A STUDY ON TRIGLYCERIDE GLUCOSE INDEX

AS A MARKER OF INSULIN RESISTANCE

A Dissertation Submitted to

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GOVERNMENT KILPAUK MEDICAL COLLEGE &

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May – 2018

BONAFIDE CERTIFICATE

This is to certify that this dissertation title **"A STUDY ON TRIGLYCERIDE GLUCOSE INDEX AS A MARKER OF INSULIN RESISTANCE"** submitted by **Dr. PRIYADARSHINI. R** to the faculty of General Medicine, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch I General Medicine, is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

I, **Dr. PRIYADARSHINI.R,** solemnly declare that the dissertation titled **"A STUDY ON TRIGLYCERIDE GLUCOSE INDEX AS A MARKER OF INSULIN RESISTANCE"** has been prepared by me under the guidance of **Prof. Dr. T.S. SANTHI, M.D.,** Department of General Medicine. This is submitted to **"The Tamil Nadu Dr. M.G.R. Medical University, Chennai"** in partial fulfillment of the requirement for the award of **MD Degree Branch I (General Medicine).**

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Date:

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INSTITUTIONAL ETHICS COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
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Protocol ID. No.06/2017 Meeting held on 03.03.2017

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "**Triglyceride Glucose Index as a Marker of Insulin Resistance** " submitted by Dr.R.Priyadarshini, M.D. General Medicine, PG Student, GKMC, Chennai-10

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

22/3/17

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My Comp<E Colon< ME 1 Sec> Ethical Committee

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ABBREVIATIONS

CVD	-	CARDIOVASCULAR DISEASE
IR	-	INSULIN RESISTANCE
ICMR	-	INDIAN COUNCIL OF MEDICAL RESEARCH
TyG	-	TRIGLYCERIDE GLUCOSE INDEX
HOMA	-	HOMEOSTATIC MODEL ASSESSMENT
HLA	-	HUMAN LEUCOCYTE ANTIGEN
NMR	-	NUCLEUR MAGNETIC RESONANCE
OGTT	-	ORAL GLUCOSE TOLERANCE TEST
CD	-	CLUSTER OF DIFFERENTIATION

CONTENTS

INTRODUCTION

"Diabetes Mellitus is a complex metabolic disorder, which results from absolute or relative deficiency in insulin secretion and or its action"[1]. There has been a continuous increase in the global prevalence of diabetes and its devastating effects on life expectancy and quality of life of individuals.

Diabetes is a major health issue in most of the South East Asian countries, especially in India where carbohydrates form the bulk of staple food Sedentary life style and decrease in day to day physical activities along with high calorie junk foods which is popular among the youth is another important factor in the increase in trend of diabetes world wide. Every second individual in the world will be affected by diabetes soon.

India has the largest diabetic population in the world and is infamously dubbed as "The Diabetic capital" of the world. According to Indian council of Medical Research (ICMR), India is faced with galloping diabetes epidemic, approximately more than 70 million patients are affected with diabetes in India and this number is projected to cross beyond hundred million by the year 2030[2-4].

Type 2 diabetes mellitus has foremost clinical and social, impact, but its causal pathophysiology is below par to be understood. Since the disease is diagnosed as a disorder of carbohydrate metabolism, i.e.,

hyperglycemia, the possible contribution of abnormal lipid metabolism to its etiology has been largely overlooked[5-6]. The predominant, obesity-related form of diabetes is characterized by hyperinsulinemia, resistance to insulin-mediated glucose disposal in skeletal muscle, and elevated plasma free fatty acid and triglyceride levels. It has been suggested that a derangement of lipid metabolism is an early event contributing to the development of both hyperinsulinemia and insulin resistance.

Insulin resistance (IR) involves reduced muscle and adipose tissue sensitivities to insulin and reduced ability of the liver to suppress hepatic glucose production and output. IR is considered a major ri.sk factor for type 2 diabetes and cardiovascular diseases (CVD)[6-8]. Because of the clinical importance of IR, the ability to identify individuals with IR before the development of cardiometabolic diseases is of paramount importance. Although the hyperinsulinemic euglycemia clamp remains the gold standard for measuring IR, its practical clinical application is limited by the labor intensiveness and cost and by ethical concerns[9]. Therefore, a simple, reliable, and reproducible index for measuring IR is urgently required.

It has been demonstrated that the product of Triglyceride (TG) and Fasting Plasma Glucose (FPG) levels Triglyceride Glucose Index (TyG-index) presents moderate power as a surrogate marker for estimating IR.

The superiority of the TyG index in identifying IR was also reported in many other studies. With these findings, a highly efficient substitute measure to establish IR can be easily applied in our clinical settings to measure the same in large scale of population where impending diabetes is at a escalating trend.

AIMS AND OBJECTIVES

1. To evaluate TyG index as a surrogate method for estimation of Insulin Resistance (IR) and as an accessible tool for assessment of IR in clinical practice.

2. To establish TyG index's correlation with adiposity, metabolic and atherosclerosis markers related to IR and its agreement with fasting insulin assay through HOMA-IR.

REVIEW OF LITERATURE

Type 2 diabetes is one of the major distressing non-communicable diseases worldwide, which shows an increasing prevalence especially in developing countries like India. Diabetes is a “Metabolic cum Vascular disorder” causing long term damage and dysfunction, which leads to failure of various organs like kidneys, eyes, heart and blood vessels[10-14].

Even after decades of insulin discovery, diabetic patients still have a considerably reduced life expectancy despite a significant decrease in incidence of acute metabolic events like ketoacidosis. This is mainly due to long term macrovascular and microvascular complications. Among non-communicable diseases, growth of diabetes appears to dramatic and worrisome.

METABOLIC SYNDROME

The metabolic syndrome has taken a prime role in relationship with diabetes mellitus. Pradhan et al (2007) relates this syndrome to an inflammatory basis of glucose disorders, whereas McGill, Molyneaux, Twigg, and Yue et al (2008) question whether the metabolic syndrome exists, even whether it matters when concerning T2DM. “DeFerranti and Osganian” (2007) discuss, in length, the epidemiology of pediatric metabolic syndrome and its association with T2DM. They oppose that the prevalence of this syndrome is rising in children and especially adolescents. Their fear is if not held early enough, the associated complications will happen in younger people, leading to a surge in morbidity and mortality in this age population. In any case, whether it is called syndrome X, or even the more recent name of cardiovascular syndrome, hypertension, hyperlipidemia, obesity and hyperglycemia as such relate to likely problems that have an endpoint in disability or death whether controlled in part or in whole.

The etiology of T2DM is even less well understood than the etiology of T1DM. It is genetic, but it has no role with the immune system and the genes are not located on the same HLA locus on the sixth chromosome. Indeed, there are probably many genes causing T2DM, located on several chromosomes. Some candidate genes have been

branded but most have not[15-18]. We also know that there is a strong environmental impact in the development of T2DM. The gene or genes seem to be extensive throughout the world and in every race and culture. But we see the disease is noticeable only in developed or developing countries where it is associated with increased caloric intake and decreased caloric expenditure (obesity).

Underdeveloped countries have a meagre incidence and prevalence of the disease and it happens primarily in the elderly. When these countries commence to industrialize or the people immigrate to more developed countries, a virtual detonation of diabetes occurs. How this change in lifestyle intermingles with the genetic precursor is not known.

INSULIN RESISTANCE AND OBESITY

We do discern that obesity is involved in insulin resistance and hyperinsulinemia, up till now not all obese people develop diabetes. Insulin resistance may hence not be the primary, or at least the genetic, defect. As formerly noted, there seems to be a loss of insulin secretory capability by the beta cells and a loss of beta cell mass (Florez et al., 2007). This is undoubtedly the main genetic defect[19]. When insulin resistance advances, the person without the gene can escalate insulin secretion and pay off. Those with the gene cannot compensate and cultivate a relative insulin deficiency and subsequent elevated blood glucose levels. This picture is fairly well agreed.

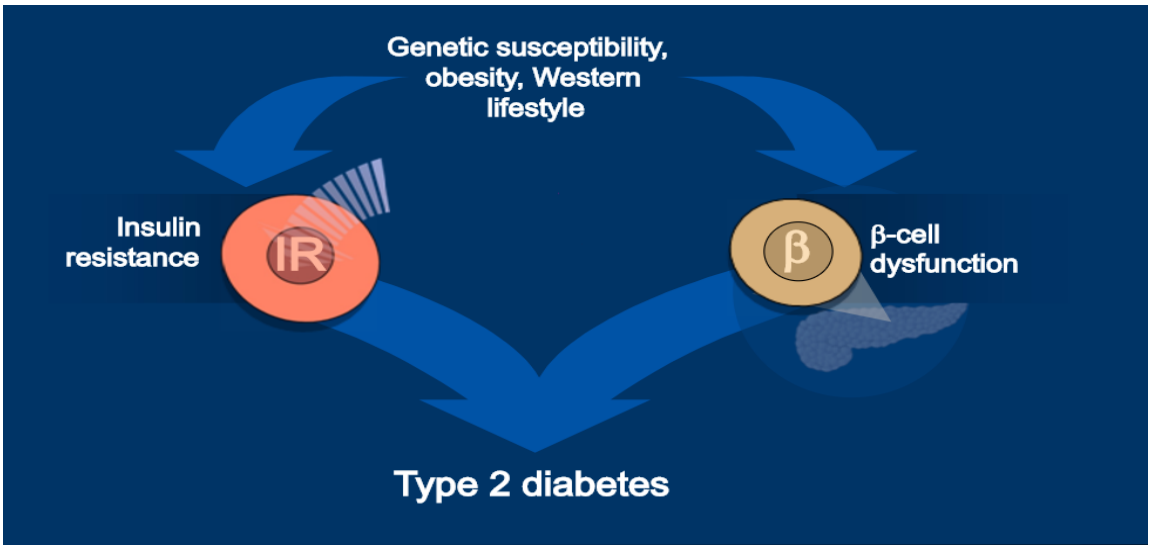
What is not understood is why?. The gene or genes for T2DM are very prevalent throughout the world and even happens in animals. If it is a detrimental gene, why has it bred in instead of being bred out over time? Perhaps it had a function. Human history is one of recurring deprivation, not the plenty we see today. The gene may have grew as a thrifty gene to develop energy utilization during times of famine. In other words, the gene sanctions us to get more miles to the gallon. During epochs of famine then, it was the individuals with the diabetic gene who endured, thus perpetuating the gene.

Today, we still see slight T2DM in countries with low caloric intake and high caloric expenditure. When those people raise their caloric intake and reduce their daily activity by improving economic conditions or migrating to developed nations, diabetes grows, often at alarming rates. The prevention key of T2DM, then, is to avoid obesity, a finding established by the Diabetes Prevention Program (Fodor & Adamo, 2001).

The generalized obesity is not associated with T2DM, rather centralized obesity does. Not only central[20-22], it is also primarily intra-abdominal obesity. Fat tissue was once assumed to be inactive tissue, is now notorious as an active organ generating many hormones and cytokines. Some of these hormones like leptin, are useful. They weaken appetite and boosts metabolism and insulin consumption. Other substances manufactured by fat tissue are unsafe specially in increasing food intake causing insulin resistance. Subcutaneous fat liable to produce good substances, and intra-abdominal fat the destructive substances. Much research remains to be done on fat hormones. This is a fruitful area of research that may clue to better treatments in upcoming days. Genetic defects in diabetes may lead to the production of abdominal fat as well as reduced beta cell function and mass. The insulin resistance of diabetes may also be produced by genetic defects in insulin receptors on cells

and/or the cascade of kinase reactions inside the cells. This remains to be established.

The recognition of presence of metabolic syndrome has developed over last 3 decades following narration of an insulin resistance syndrome or syndrome x in 1988.



PATHOGENESIS OF INSULIN RESISTANCE

- Resistance to the action of insulin is the central feature of metabolic syndrome.
- Liver, skeletal muscle and adipose tissue are considered as major insulin responsive tissues, but vascular system can also be considered as an insulin response organ.
- In metabolic syndrome, insulin resistance is linked predominantly to a cluster of disorders involving triglyceride and glucose

metabolism, increased blood pressure and vascular inflammation given that insulin resistance is fundamental to a diagnosis of the syndrome, an understanding of the cause and consequences of insulin resistance is crucial to understanding of pathogenesis of metabolic syndrome.

- Decreased level of physical activity and increased dietary caloric intake adversely affects the metabolic profile by decreased free fatty acid and glucose oxidation in skeletal and Cardiac muscle which potentially contributes to body fat accumulation and resistance to biological action of insulin secondary to many cytokines secreted by adipose tissue like TNF alpha, IL-6, IL-1beta.[24-30]

Increased TNF -alpha leads to

1) Decreases insulin induced suppression of hepatic glucose production

2) Increased free fatty acid and cholesterol synthesis.

3) Increased hepatic VLDL production and increased adipocyte lipolysis leading to increased non estero fixed free fatty acid (NEFAs) which stimulates hepatic triglyceride synthesis and increased VLDL assembly and secretion.

Increased TNF-alpha probably contributes to the classical dyslipidemia associated with metabolic syndrome and type 2diabetes (i.e) Increased plasma triglycerides, decreased HDL cholesterol, increased LDL cholesterol all as well contributing to increased plasma glucose.[31-32]

OTHER CONTRIBUTIONS :

1) Within vasculature metabolic syndrome is also associated with increase in cellular reactivity.

Endothelial cell, platelets, monocytes gets activated.

Reactive cells predispose an individual to pro coagulant and proinflammatory vascular phenotype

Probably preceded development of atheromatous plaques

2) Immune response - undoubtedly involved in developing an atheromatous plaque

- Within the plaque, the T helper cells predominantly TH1 cells secrete proinflammatory cytokines.

- With marked hyperlipidemia there is a shift TH2 cells noted. It secretes anti inflammatory cytokines.

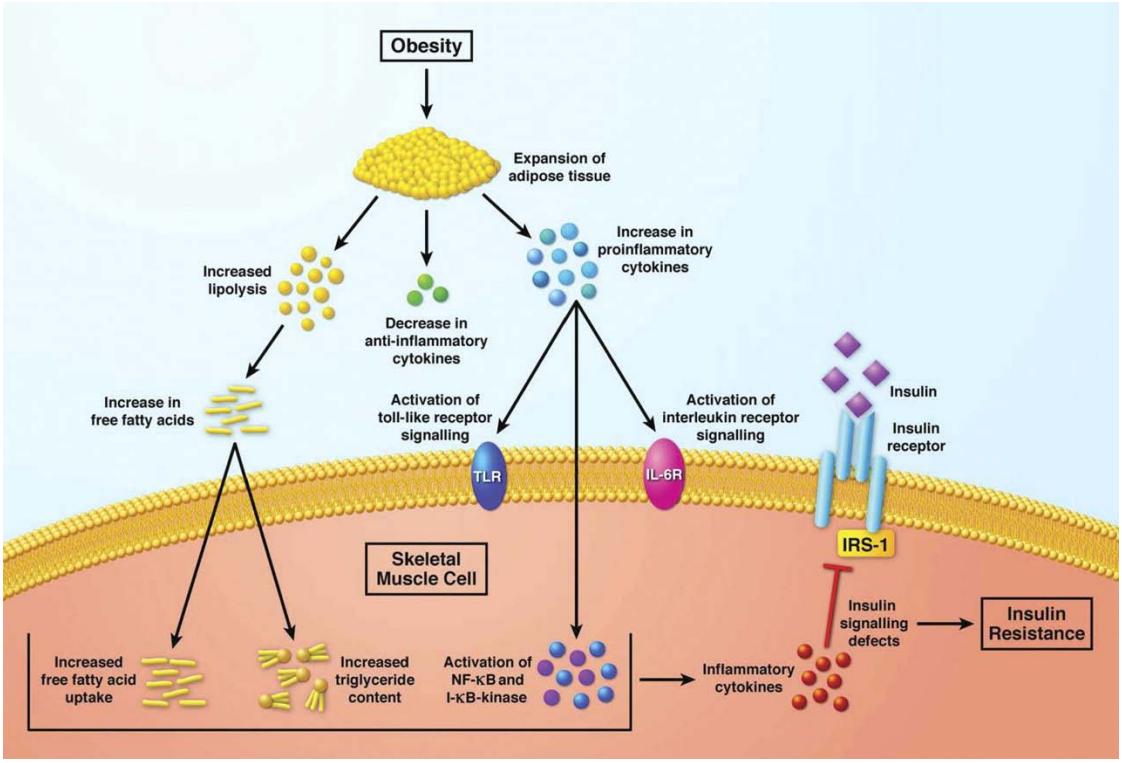
- Whether this finding represents a part of causal pathway, is a consequence of inflammatory disease or represents physiological healing is uncertain.

3) Insulin resistance leads directly to endothelial dysfunction, Impaired endothelial dependent vasodilation in response to acetylcholine, Increased expression of adhesion molecules like ICAM -1 and VCAM-1 which binds to various classes of leukocytes, secondary to proinflammatory cytokines[33-36].

4) Adiponectin

Recently described molecule that may be important in pathogenesis of metabolic syndrome. Secreted exclusively by adipocytes has high affinity for adiponectin receptors expressed in two other insulin sensitive tissues namely skeletal muscles and liver. In transgenic mice in which adiponectin gene is knocked out, adiponectin deficiency caused diet induced glucose intolerance, insulin resistance and increased NEFA*

Thus net effect of increased adiponectin signalling is increased fatty acid oxidation increased glucose utilisation reduced endogenous glucose production and decreased inflammation.

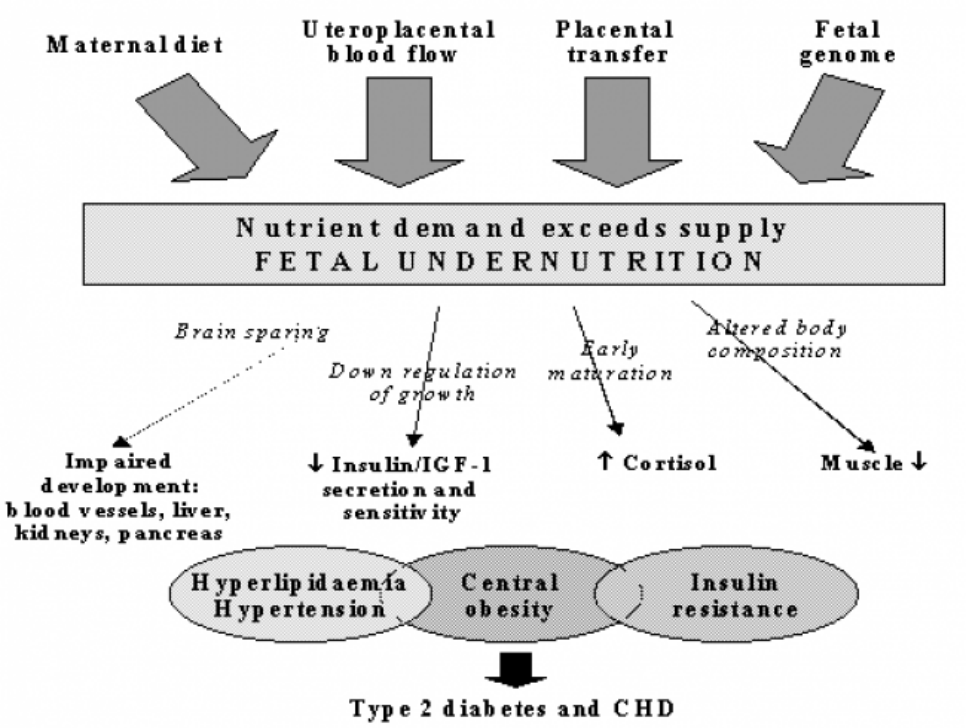


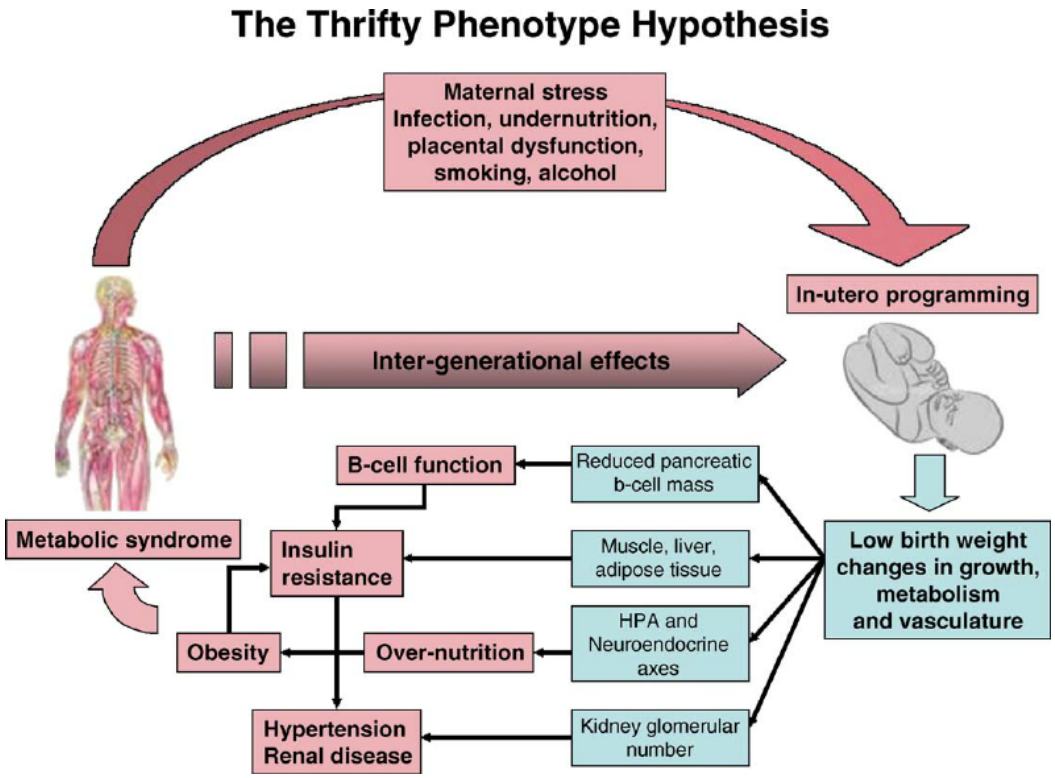
THRIFTY PHENOTYPE HYPOTHESIS[37-39]:

This hypothesis states that in response to a poor fetal nutrition the compromised fetus will adopt a number of strategies to maximize its chances to survive post nataly.

Firstly, growth of brain is spared at the expense of other tissues like muscle, kidney and exocrine pancreas, in addition metabolic programming is proposed to occur in a manner beneficial to survival under oddities of poor postnatal nutrition.

No problems arises if fetus is born in to condition of poor postnatal nutrition . Eg. rural Tanzania however problems are proposed to occur if fetus is born in to conditions of adequate or over nutrition.


Maternal diet
Uteroplacental blood flow
Placental transfer
Fetal genome
Nutrient demand exceeds supply
FETAL UNDERNUTRITION
Brain sparing
Down regulation of growth
Early maturation
Altered body composition
Impaired development: blood vessels, liver, kidneys, pancreas
↓ Insulin/IGF-1 secretion and sensitivity
↑ Cortisol
Muscle ↓
Hyperlipidaemia Hypertension
Central obesity
Insulin resistance
Type 2 diabetes and CHD


The Thrifty Phenotype Hypothesis
Maternal stress Infection, undernutrition, placental dysfunction, smoking, alcohol
In-utero programming
Inter-generational effects
B-cell function
Reduced pancreatic b-cell mass
Metabolic syndrome
Insulin resistance
Muscle, liver, adipose tissue
Low birth weight changes in growth, metabolism and vasculature
Obesity
Over-nutrition
HPA and Neuroendocrine axes
Hypertension Renal disease
Kidney glomerular number

So it is clear now that Insulin resistance (IR) is a central feature in the natural history of type 2 diabetes. The ability to accurately measure IR is therefore of substantial importance for chronic disease researchers. IR can be quantified using detailed physiological protocols.

METHODS FOR MEASURING INSULIN RESISTANCE [41-46].

Some of the available methods are:

- **THE HYPERINSULINEMIC EUGLYCEMIC GLUCOSE CLAMP TECHNIQUE[47-49]:**

The "gold standard" for calculating. insulin sensitivity in vivo because it directly measures the effects of insulin to promote glucose utilization under steady state conditions.

In this method after an overnight fast of at least 10 h, subjects were and placed in a recumbent position. An iv catheter was placed in antecubital vein for infusion of insulin, glucose, and potassium phosphate. Another catheter was placed in the contralateral hand for blood sampling. The hand used for sampling was warmed with a heating pad to arterialize the blood. An insulin solution (regular) was prepared with normal saline at a concentration ranging from 0.8–1.2 U/ml. The insulin solution was allowed to dwell in the iv lines for at least 15 min, and the lines were then flushed before the beginning of the insulin

infusion. Insulin was infused at 120 μU/m2/min for 4 h using a calibrated syringe. pump A solution of potassium phosphate was infused at the same time (0.23 mEq/kg/h) to prevent hypokalemia. Blood glucose concentrations were measured at the bedside every 5–10 min using a glucose analyzer and an infusion of 20% dextrose was adjusted to maintain the blood glucose concentration at the fasting level. Blood samples were also collected every 20–30 min for determination of plasma insulin concentrations. The steady state period of the clamp was defined as a 60-min or longer period (at least 1 h after the beginning of the insulin infusion) during which the coefficient of variations for blood glucose, plasma insulin, and glucose infusion rate were less than 5%.

The glucose clamp-derived index of insulin sensitivity was defined as.

$$\frac{M}{G3\ DI}$$

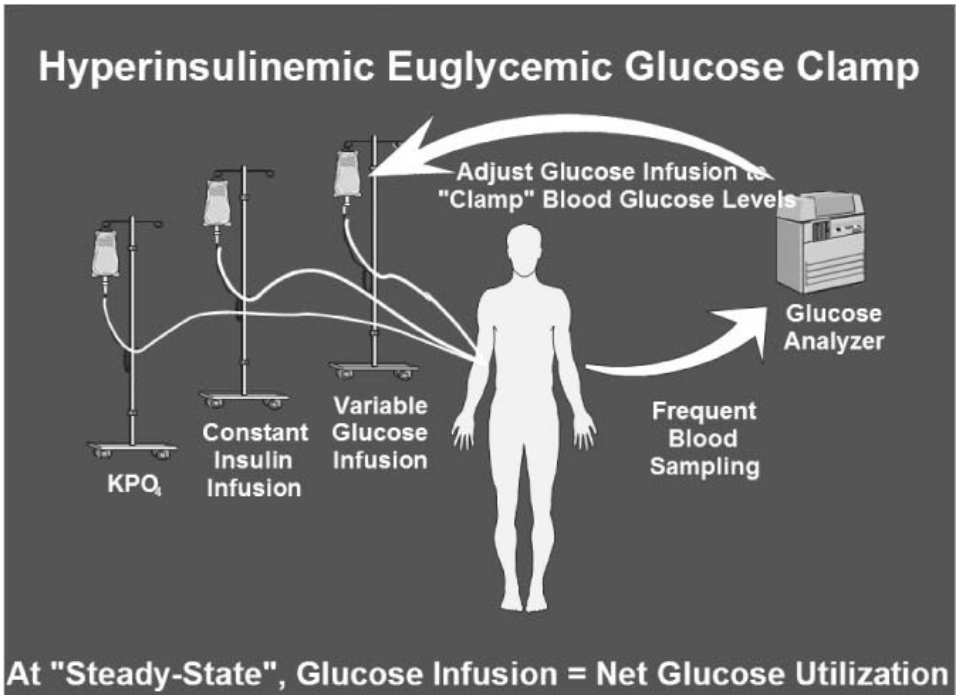
*corrected for body weight

Where M is the steady state glucose infusion rate (mg / mt),

G is the steady state blood glucose concentrations (mg / dL)

DI is the difference between basal and steady state plasma insulin concentrations (μU / mL)

However, the glucose clamp is not easily applied in large scale investigations because iv infusion of insulin, frequent blood samples over a 3-h period, and continuous adjustment of a glucose infusion are required for each subject studied.



- **FREQUENTLY SAMPLED IV GLUCOSE TOLERANCE TEST (FSIVGTT)** [50-52].

A well accepted alternative for estimating insulin sensitivity. Although this approach is less labor intensive than the glucose clamp, the FSIVGTT is still not ideal for large studies because it requires obtaining approximately 30 blood samples over 3 hours. Furthermore., although the minimal model index of insulin sensitivity (SIMM) generally correlates well with measurements of glucose clamp tests, identification. of SIMM in subjects with impaired insulin secretion (e.g. patients with diabetes) is

problematic often. Moreover, recent studies have demonstrated systematic errors in minimal model estimates of glucose effectiveness and insulin sensitivity that may be due to oversimplified model representations of physiology [13–15].

- **QUANTITATIVE INSULIN SENSITIVITY CHECK INDEX (QUICKI)[53-55].**

  A novel index that can be determined from a fasting blood sample.

$$\textbf{QUICKI} = \frac{1}{[\log(I0) \times \log(G0)]}$$

where I_0 is the fasting insulin, and G_0 is the fasting glucose. Importantly, QUICKI could be identified for all study subjects, and the correlation of QUICKI with glucose clamp measures of insulin sensitivity was significantly better than the correlation between SIMM and the glucose clamp. These methods, however, are excessively complex, invasive, and costly for use in large observational. epidemiological studies.

All three of these tests require intravenous infusions and are therefore relegated almost exclusively to research settings.

- **FASTING INSULIN RESISTANCE INDEX (FIRI)** [53,56]

A product of plasma insulin and glucose (normalized to an expected glucose of 5 mmol/l and insulin of 5 mU/l to give a reference range centered around unity).

FIRI = fasting glucose X fasting insulin/25

In a set of newly diagnosed type 2 diabetics FIRI positively correlated with triglyceride and inversely with high-density lipoprotein (HDL) cholesterol. However no relations were observed between lipid profile and fasting glucose, the glucose: insulin ratio, or HbA1c. Fasting insulin had a good correlation with HDL but very poorly with triglyceride (r=0-22, p=02). A near perfect linear relation was noted between FIRI and insulin resistance as estimated by the HOMA-IR parameter of the homoeostasis model Assessment of [121] Matthews et a1.

Consequently, a number of simple (surrogate) indexes have been proposed for projects that require the estimation of IR in large numbers of subjects. These indexes use either transformations or weighted combinations of insulin or insulin and glucose concentrations in the fasted state and at various times during the oral glucose tolerance test (OGTT). Some have been developed using mathematical modeling of the direct measures mentioned above.

Several surrogate indices, including the Matsuda index, are based on dynamic measures of glucose and insulin at different time points

during an oral glucose tolerance test. Because they require several hours of patient monitoring, clinical use is uncommon.

MEASUREMENTS CONDUCTED ON FASTING PLASMA SAMPLES

More amenable for routine clinical use.

- **HOMEOSTASIS MODEL ASSESSMENT OF INSULIN RESISTANCE (HOMA-IR)[57-60]:**
- The most widely employed, which uses fasting glucose and insulin levels.
- The HOMA-Index is calculated based on the values of basal insulin and glucose in plasma. This index brings out the ability of basal insulin to suppress hepatic glucose production in fasting conditions and thus reflects mainly insulin resistance in the liver[9].
- **HOMA-Index is calculated as**

$$\frac{\text{fasting plasma glucose (mmol/ml)} \times \text{fasting serum insulin (µU/ml)}}{22.5.}$$

(Or)

$$\frac{\text{fasting plasma glucose (mg/dl)} \times \text{fasting serum insulin (µU/ml)}}{405}$$

- Due mainly to biological variability requiring repeat testing and lack of insulin assay standardization, HOMA-IR continues to be used more for research than for clinical applications.

1) TGs/HDL-C ratio[61-62]

Among the earliest manifestations of IR, observed well in advance of the diagnosis of diabetes or prediabetes, are alterations in metabolism of lipid and lipoprotein causing escalations in triglycerides (TGs) and regression of high-density lipoprotein cholesterol (HDL-C).

McLaughlin and colleagues on the basis of this, pointed that the TGs/HDL-C ratio could provide a more simple and clinically accessible. alternative to glucose and insulin measurements for identifying insulin resistance in overweight and obese patients.

2) Lipoprotein Insulin Resistance Index (LP-IR)

Nuclear magnetic resonance (NMR) spectroscopy provides a more clearcut and refined assessment of the lipoprotein abnormalities associated with IR. In specific, the insulin-resistant individuals have higher levels of large subclass of very-low-density lipoprotein particles (VLDL-P) and the small subclass of low density lipoprotein particles (LDL-P) and yet lower levels of the large subclass of HDL particles (HDL-P). In addition, mean VLDL particle. Sizes are generally greater

and mean LDL and HDL sizes are smaller in IR or prediabetic patients. Clinical NMR testing is highly used to bring the LDL and HDL particle concentrations to aid in CVD risk management. Because the same NMR measurement, as it also provides the lipoprotein subclass and size information linked to IR, we sought to develop a composite Lipoprotein Insulin Resistance Index (LP-IR) to assess a patient's IR status.

3) TRIGLYCERIDE GLUCOSE INDEX :

The TyG-Index is even simpler to calculate, based on the product of plasma triglycerides and glucose. A possible increase in triglycerides in plasma would seem able to interfere with the normal metabolism of glucose in the muscle, thereby producing a low sensitivity to insulin. Henceforth, this index, unlike HOMA-Index, seems to mirrorize mainly muscle insulin resistance.

TyG-Index is calculated as

$$\textbf{Log}\left\{\frac{\textbf{fasting triglycerides (mg/dl) X fasting glucose (mg/dl)}}{\textbf{2}}\right\}$$

The TyG-Index, unlike HOMA-Index, had a significant association with carotid atherosclerosis, despite adjusting all traditional cardiovascular risk factors. Indeed, the TyG-Index remained in the model

eventhough the components of the Metabolic syndrome or the presence of the syndrome was excluded.

DERIVED SURROGATE MARKERS

S No	Method	Measurement	Comments
1	Matsuda index	10 000/$\sqrt{}$ (fasting G × fasting I) (mean G × mean I)	Represents both hepatic and peripheral tissue sensitivity to insulin
2	Gutt index	75 000 + (G_0 - G_{120}) (mg/dL) × 0.19 × BW/120 × $Gmean_{(0, 120)}$ (mmol/L) × Log [$Imean_{(0, 120)}$] (mU/L)	Good to predict onset of type 2 diabetes
3	Stumvoll index	0.156 - 0.0000459 × I_{120} (pmol/L) – 0.000321 × I_0 (pmol/L) – 0.00541 × G_{120} (mmol/L)	Utilizes demographic data like age, sex and BMI along with plasma glucose and insulin to predict insulin sensitivity
4	Avignon index	Sib = 10^8/(I_0 (mU/L) × G_0 (mmol/L) × VD) Si2h = 10^8/(I_{120} (mU/L) × G_{120} (mmol/L) × VD]	Determines glucose tolerance and insulin sensitivity in single test
5	Oral glucose insulin sensitivity index	G and I concentrations from a 75 g OGTT at 0, 2, and 3 h (3 h OGTT) or at 0, 1.5, and 2 h (2 h OGTT). The formula includes six constants	
6	Log (HOMA-IR)	Evaluates insulin resistance in insulin-resistant states like glucose intolerance and mild to moderate diabetes	

Sib: Derived from fasting plasma insulin and glucose; Si2h: Derived from fasting plasma insulin and glucose ant 2 h of OGTT; OGTT: Oral glucose tolerance test.

MATSUDA INDEX

A very simple to calculate, easy and a novel assessment of insulin sensitivity which provides a reasonable approximation of whole-body insulin. Sensitivity from the OGTT was developed by Matsuda and Defronzo, referred to as the "Matsuda index"[63]. Here the OGTT index of insulin sensitivity [ISI (composite)] was calculated using both the data of the entire 3 h OGTT and the first 2 h of the test.

The composite "WHOLE-BODY INSULIN SENSITIVITY INDEX" (WBISI), developed by Matsuda and DeFronzo is based on insulin values given in microunits per millilitre (μU/mL) and those of glucose, in milligrams per decilitre (mg/dL) obtained from the OGTT and the corresponding fasting values.

"WBISI" is calculated as

$$\frac{10\,000}{\sqrt{(\text{fasting glucose} \times \text{fasting insulin})(\text{mean glucose} \times \text{mean insulin})}}$$

This index is a composite representative of both hepatic and peripheral tissue sensitivity to insulin.

GUTT INDEX

Gutt et al[64] also tried OGTT values in order to develop an easy measure of insulin sensitivity. A formula for an insulin sensitivity index, ISI (0, 120), that made use of the (fasting) 0 minute and 120 minute post-oral glucose (OGTT) insulin (I) and glucose(G) concentrations along with body weight (BW) was devised.

$$ISI_{(0,\,120)} = \frac{75\,000 + (G_0 - G_{120}) \times 0.19 \times BW}{120 \times Gmean_{(0,\,120)} \times Log\,[Imean_{(0,\,120)}]}$$

Insulin concentration is expressed in mU/l and glucose concentration is expressed as mg/dL in the numerator and mmol/l in the

denominator. It correlated well with the insulin sensitivity index obtained from the euglycemic hyperinsulinemic clamp.

STUMVOLL INDEX

Stumvoll et al[65] proposed use of demographic data such as age, sex and body mass index (BMI) in addition to plasma glucose (mmol/L) and insulin (pmol/L) responses during the OGTT to predict. insulin sensitivity. and beta cell function.

$$\mathbf{ISI_{Stumvoll} = 0.156 - 0.0000459 \times I_{120} - 0.000321 \times I_0 - 0.00541 \times G_{120}}$$

$$\mathbf{ISI_{Stumvoll} = 0.222 - 0.00333 \times BMI - 0.0000779 \times I_{120} - 0.000422 \times Age}$$

The metabolic clearance rate of glucose and ISI calculated by this method included BMI, insulin (120 min), and glucose (90 min).These parameters correlated better with the measured parameters than the homeostasis. model assessment for secretion and resistance.

AVIGNON INDEX

Avignon et al[66]tried to equate IS indices which was a derivative from plasma insulin (I) (mU/L), glucose (G) (mmol/L) and apparent glucose distribution volume in the basal state (Sib), and at the end of second hour OGTT (Si2h). Another insulin sensitivity index (SiM) was designed by averaging Sib and Si2h.

$$SiM = \frac{[(0.137 \times Sib) + Si2h]}{2}$$

where $Sib = \frac{10^8}{(I_0 \times G_0 \times VD)}$ and $Si2h = \frac{10^8}{(I_{120} \times G_{120} \times VD)}$

(VD is an estimate of the apparent glucose distribution volume)

It was witnessed that the results gained by computation of sensitivity indices from G and I concentrations in the basal state and during a conventional 2 h OGTT were useful for merging both a determinating glucose tolerance and estimating insulin sensitivity in a solitary and modest test.

ORAL GLUCOSE INSULIN SENSITIVITY INDEX

The oral glucose insulin sensitivity index requires glucose and insulin concentrations from a 75 g OGTT at 0, 2, and 3 h (3 h OGTT) or at 0, 1.5, and 2 h (2 h OGTT). The formula includes six constants adjusted to match the clamp outcomes. This is confirmed against the clamp method in patients with IGT and type 2 diabetes[67].

Log (HOMA-IR)

In the case of persistently deranged β-cell function, HOMA-IR may not give an appropriate method to estimate IR. The coefficient of variation for HOMA-IR fluctuates greatly, depending upon the number of fasting samples attained and the type of insulin assay used[68-71]. Log

(HOMA-IR) changes the skewed distribution of fasting insulin values to determine a much stronger linear correlation with glucose clamp estimates of insulin sensitivity when extensive ranges of insulin sensitivity/resistance. are being studied.

Log (HOMA) is being functional largely in epidemiological studies, and in clinical research studies.

IMMINENT MARKERS

With the passing of time and continuous increased research, many more recent contaminants are gaining attention as surrogate indicators in evaluation of IR. These days, inflammation related indicators have became popular in terms of evaluation of blood insulin resistance.

S No	Marker
1	Insulin growth factor binding protein-1 (IGFBP-1)
2	sCD36 (solubleCD36)
3	C-reactive protein (CRP)
4	Ferritin
5	Adiponectin
6	Tumour necrosis factor (TNF alpha)
7	Resistin
8	C3 complement
9	Glycosylated hemoglobin (Hb)A1c
10	Protein kinase C (PKC) in microangiopathy
11	Sex hormone-binding globulin (SHBG) in hyperandrogenic syndrome

INSULIN GROWTH FACTOR BINDING PROTEIN-1

Recent research has suggested insulin growth factor binding protein-1 (IGFBP-1) as a novel and a potential plasma marker to assess insulin resistance. IGFBP-1 has been found to have a good relationship with FSIVGTT valuation of insulin sensitivity, mainly in children younger than 10 years[72]. However, more studies are necessary to substantiate the utility of this marker. IGFBP-1 levels weakens with obesity and IR. Although raised fasting insulin is less sensitive but more specific, it has been proposed that in young subjects, IGFBP-1 might act as a suitable and vulnerable marker of IR. It is an emerging marker which may be useful in this context.

SOLUBLECD36

"Macrophage CD36" is a crucial proatherogenic molecule that hunts oxidized low-density lipoprotein, causing foam cell formation. Raised blood sugar and altered macrophage insulin signaling in insulin resistance primes increased expression of CD36[73]. SolubleCD36 has been stated to be noticeably higher in patients with type 2 diabetes and insulin resistance.

It is claimed that it might denote a potential marker of IR and its complications.

C-REACTIVE PROTEIN

C-reactive protein (CRP) is one of the finest studied markers for systemic subclinical inflammation, and may have prognostic value in envisaging the upcoming risk of cardiovascular happenings[74]. In cross-sectional studies, highly sensitive - CRP has been found to relate with raised triglyceride, reduced HDL, raised blood pressure and hiking fasting plasma glucose concentrations, signifying its association with augmented prevalence metabolic syndrome associated with IR[75,76]. Few studies have recognized the relationship of CRP with IR irrespective of obesity[77].

In a latest study, CRP was found to considerably associate with numerous surrogate measures of IR like fasting insulin, McAuley index, the Raynaud index, QUICKI, quantitative insulin sensitivity check index, Homeostatic model assessment, the Insulin: glucose ratio and Avignon index in non-diabetics[78]. Because of the ease of measurement, steadiness, and better-quality high-sensitivity method, CRP may be suitable as a clinical measure for detecting individuals at risk for IR[79].

FERRITIN

Ferritin is the key intracellular iron storage protein. Of late it has been put forward that when markers of the iron metabolism are raised, the

incidence of the metabolic syndrome is higher[80]. Ferritin has been linked up with both hyperinsulinemia and hypertriglyceridemia. Metabolic disorders are common amid patients with high ferritin without genetic hemochromatosis compared to those with genetic hemochromatosis. Iron deposition in various tissues disturbs insulin sensitivity and function, thereby producing insulin resistance and inflammation.

A few studies have confirmed a bond among markers of insulin resistance (HOMA-IR, fasting insulin) and ferritin[81]. Fumeron et al[82] also noticed that plasma ferritin concentrations certainly correlate with fasting insulin and fasting glucose.

ADIPONECTIN

Adiponectin is a multifunctional protein that employs pleiotropic insulin-sensitizing effects and therefore considered as a prime molecule in the pathogenesis of metabolic syndrome. It reduces hepatic glucose production and raises up glucose uptake and fatty acid oxidation in skeletal muscle. Adiponectin levels are reduced in obesity and are negatively correlated to insulin-resistant states and high-sensitivity CRP levels.

Unbalanced levels of adiponectin have been related to insulin resistance. Adiponectin has a sturdier negative correlation with HOMA in

individuals without the metabolic syndrome when compared to those with metabolic syndrome.

Several forthcoming studies have confirmed that hypo adiponectinemia was associated with a raise in insulin resistance and an higher risk of evolving diabetes[83-91].

TUMOUR NECROSIS FACTOR ALPHA

Several studies have been piloted to discover the role and use of tumour necrosis factor (TNF) to help in measuring the IR. TNF has been verified to have a relation to insulin resistance measured by HOMA-IR[92] or metabolic syndrome status[95] and to insulin clamp[93,94]

RESISTIN

The relationship between resistin and insulin resistance in humans has not been fully proven. Many studies have been failed in making out an association between resistin and measures of insulin resistance[96,97]. On the contrary, a few studies have been directed which have indeed revealed a substantial relationship between IR (HOMA-IR) and resistin[88,98-100].

C3 COMPLEMENT

The chief activation fragment of C3, C3a desArg (acylation stimulating protein) helps glucose transmembrane transport and the production of triglycerides in adipocytes. This advocates that it has insulin-like properties[101]. C3 is intensely associated with insulin resistance (as defined according to the homeostasis model assessment (HOMA), irrespective of the components of the metabolic syndrome[102]. The strong association of C3 with insulin action and fasting insulin has been described in young adult Pima Indians[103].

GLYCOSYLATED HEMOGLOBIN

Glycosylated hemoglobin (HbA1c) has been used to analyse extended-term glycemic control in diabetics. However, its part and clinical value in patients suffering from IR or metabolic syndrome in nondiabetic subjects is uncertain. HbA1c has been offered as a measure of surrogate assessment of metabolic syndrome, thereby estimating IR because of various influences. HbA1c mirrors long-term glycemic control in diabetic patients and is a noteworthy forecaster of long-term complications of diabetes[104,105]. Though HbA1c cannot be considered as a screening or diagnostic tool for diabetes, it has been verified that HbA1c symbolizes both fasting and postprandial glycemic states[106-111].

Upper normal levels of HbA1c in the range of 5.7%-6.4% have been found to reverberate some components of insulin resistance syndrome or metabolic syndrome[112]. A study steered in the nondiabetic, obese, first-degree relatives of African-Americans, genetically predisposed to type 2 diabetes[112] showed meaningfully high HOMA IR, reduced insulin sensitivity and reduced glucose effectiveness in the non diabetic study group. Insulin sensitivity and glucose effectiveness were analyzed and measured and using Bergman's Minmod software program[113,114].

It has been hypothesized that HbA1c can be considered as a foreteller of insulin resistance.

PROTEIN KINASE C IN MICROANGIOPATHY

It has been guessed that activation of the protein kinase C b isoform (PKCb) which is facilitated by hyperglycemia acts as a potential surrogate marker for microangiopathic diseases, and diabetic retinopathy in specific[115]. A study done on diabetics correlated PKC activation and diabetic retinopathy. It was proposed that PKC activation in mononuclear cells may serve as a surrogate marker for diabetic microangiopathy[115].

SEX HORMONE BINDING GLOBULIN IN HYPERANDROGENIC SYNDROME

Sex hormone-binding globulin (SHBG) serves as a predictive marker of IR in obese women with hyperandrogenic syndrome. In a study done by Kajaia et al[116], IR was proven by means of the Matsuda ISI in hyperandrogenic women, who were found to have potentially lower SHBG and HDL levels. SHBG may be considered as an predictive marker in these types of cases.

METHODOLOGY

- **STUDY DESIGN**

Cross sectional study among newly detected type 2 diabetes patients in Department of General Medicine, kilpauk medical college, Chennai.

- **SAMPLE SIZE:**

$Z^2 * p (1 – p) / d^2$, where Z is the standard variate, p the prevalence of diabetes and d is absolute error or precision taken as 5 %

Rounded to 120

- **STUDY POPULATION :**

120 Type 2 diabetic patients, both male and female, who satisfy all inclusion and exclusion criteria, from the outpatient department of Medicine department of Government Kilpauk Medical College, Chennai, are included in this study.

- **CRITERIA:**

Inclusion criteria:

1. Newly detected type 2 diabetes mellitus

2. Patients with impaired fasting glucose

Exclusion criteria

1. Type 1 diabetes
2. Patient already on insulin or insulin sensitisers, lipid lowering drugs, steroids, antipsychotics etc.
3. Gestational diabetes
4. Secondary diabetes
5. Patient in ketoacidosis or extremely sick.

- **STUDY PERIOD**

  6 months of study from March 2017 to September 2017.

- **DATA COLLECTION METHODS**

- Data regarding medical history, lifestyle behavior and blood analyses of 120 the subjects were retrieved on the day of inclusion in the study. The recorded information from each visit included the following data:

- Personal lifestyle behavior including cigarette smoking (none, former smoker or current smoker), daily alcohol intake (yes/no) and lifestyle pattern (physically active/sedentary behavior).

- Anthropometric measurements (weight, height and BMI) and BP, which were performed by a trained nurse according to standardized methods.

- Weight was quantified with subjects wearing light clothing and to the nearest 0.1 kg; height was measured without shoes to the nearest 0.1 cm.

- BMI was calculated as the body mass divided by the square of the body height and expressed in units of kg/m2. The participants were categorized as normal weight, overweight, or obese by the commonly accepted BMI ranges.

- Prior to the BP measurement, the subjects were asked to remain seated for 5 min. The BP on the indistinctly right or left arm was measured twice with an aneroid sphygmomanometer and a stethoscope (Littman® Classic II S.E.) following the World Health Organization (WHO) criteria (Anon., 1993), and the average was recorded.

- Clinical history and relevant information about cardiovascular disease (coronary heart disease, cerebrovascular disease, peripheral arterial disease), cancer and psychiatric diseases were recorded.

- Hypertension was defined according to the basis of the WHO—International Society of Hypertension Guidelines (Anon., 1993) as ≥140 (systolic BP)/90 (diastolic 127 BP) mm Hg or when a subject reported having been prescribed antihypertensive medication.

- Waist circumference , hip circumference , neck circumference and waist hip ratio were also measured .

- Routine biochemical data including FPG, fasting insulin (done using CLIA method , for calculating HOMAIR), Total cholesterol (TC), TG, HDL cholesterol (HDL-C), and LDL cholesterol (LDL-C) and carotid Doppler (to assess intimal thickness) were also retrieved. Blood samples were drawn after an 8-h of fasting and analyzed in a central laboratory with Chemistry Analyzer under strict quality control. FPG was measured through the hexokinase method. TC, HDL-C and TG were determined using enzymatic colorimetric tests and LDL-C was calculated using 134 the Friedewald formula (Friedewald et al., 1972). We considered as missing the values of LDL-C in patients with TG levels greater than 400 mg/dl.

- The TyG index was calculated as

  ln[fasting Triglycerides (mg/dl) x Fasting glucose (mg(dl)/2].

  The TyG index is expressed by a logarithmic scale.

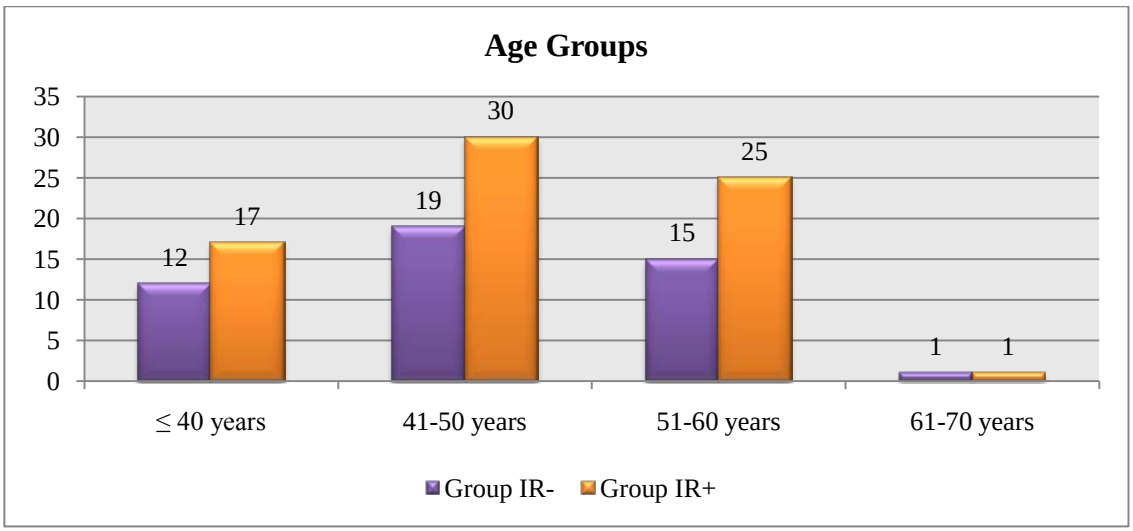
OBSERVATION AND RESULTS

In our study conducted at department of General medicine, Kilpauk Medical College 120 individuals who satisfied the inclusion and exclusion criteria are included. All persons were analysed with proforma with detailed history taking and anthropometry, vitals, system examination and require investigations were carried out. Individuals were grouped in to Insulin resistant group (Group IR +) and Insulin resistance absent group (Group IR-) according to ATPIII criteria (Individuals with 3 or more of following 5 abnormalities were considered to have insulin resistance syndrome [IRS] :

- abdominal obesity WC > 102 cm in men and > 88 cm in women
- elevated BP systolic BP >= 130 mm hg or diastolic BP >= 85 mmhg
- hypertriglyceridemia >= 1.7mmol/l
- HDL <= 1.04mmol/l in men and <1.29 mmol/l in women
- High fasting blood glucose >= 6.1mmol/l). Out of 120 subjects, 70 were males and 50 were females. 73 had signs of Insulin resistance, while 47 did not have.

Descriptive statistics was done for all data and suitable statistical tests of comparison were done. Continuous variables were analysed with the Unpaired t test/single factor ANOVA and categorical variables were analysed with chi squared test/ Fisher Exact Test. Correlation analysis done and pearsons calculated. Accuracy analysis done to calculate AUC. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS Version 16. Microsoft Excel 2010.was used to generate charts.

AGE DISTRIBUTION

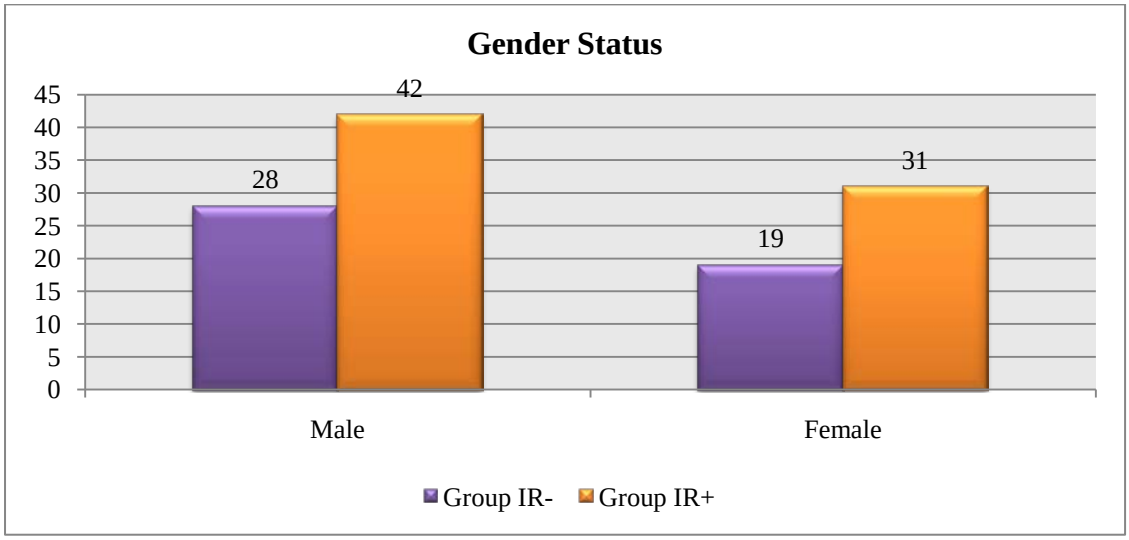


Age Groups	Group IR-	%	Group IR+	%
≤ 40 years	12	25.53	17	23.29
41-50 years	19	40.43	30	41.10
51-60 years	15	31.91	25	34.25
61-70 years	1	2.13	1	1.37
Total	47	100.00	73	100.00

Age Distribution	Group IR-	Group IR+	P value Unpaired t Test
Mean	46.26	47.26	0.4844
SD	7.42	7.81	

Majority of the study subjects in IR -ve group are distributed in 41-50 years age group (n=19, 40.43%) and same age group in IR +ve group (n=30, 41.10%) (p=0.4844, unpaired t test), thereby showing no statistical significance .

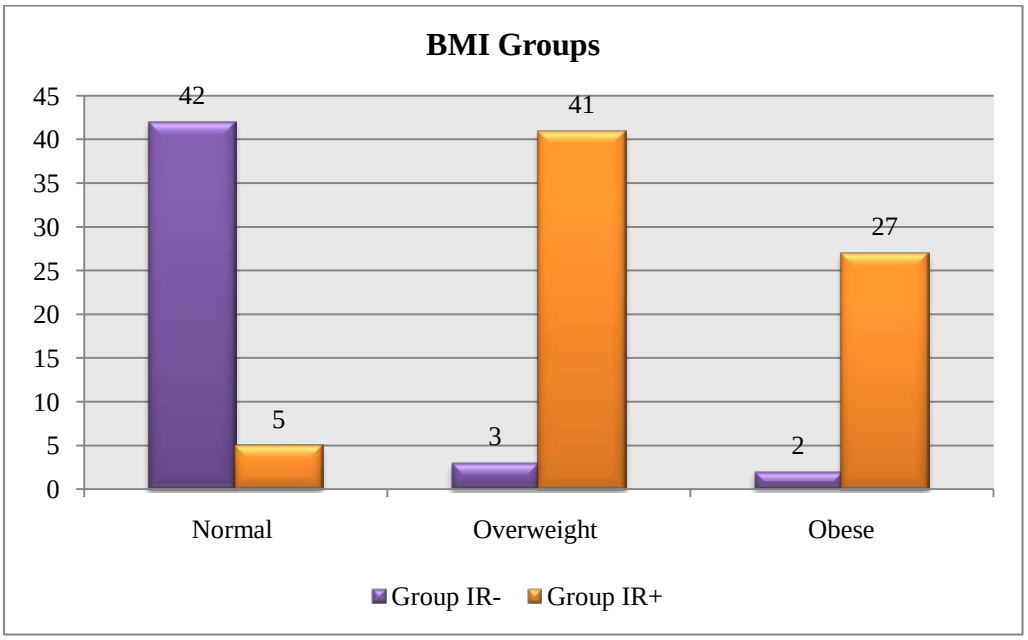
GENDER DISTRIBUTION



Gender Status	Group IR-	%	Group IR+	%	P value Chi Squared Test
Male	28	59.57	42	57.53	0.8249
Female	19	40.43	31	42.47	
Total	47	100.00	73	100.00	

Majority of the study subjects in IR -ve group are males (n=28, 59.57%) and same too in IR +ve group (n=42, 57.53%) (p=0.8249, chi square test), showing no significant statistical association.

BMI DISTRIBUTION :

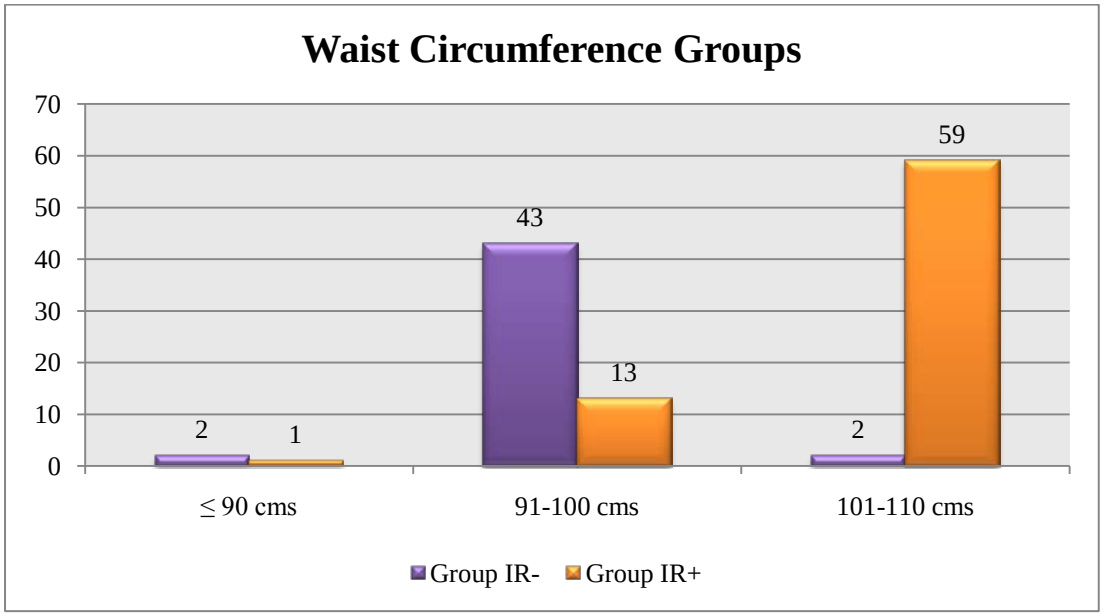


BMI Groups	Group IR-	%	Group IR+	%
Normal	42	89.36	5	6.85
Overweight	3	6.38	41	56.16
Obese	2	4.26	27	36.99
Total	47	100.00	73	100.00

BMI Distribution	Group IR-	Group IR+	P value Unpaired t Test
Mean	23.21	29.03	<0.0001
SD	2.38	2.22	

Majority of the study subjects in IR -ve group are distributed in normal BMI group (n=42, 89.35%) and overweight group in IR +ve group (n=41, 56.16%) (p= <0.0001, unpaired t test), showing a significant statistical significance.

WAIST CIRCUMFERENCE VERSUS INSULIN RESISTANCE

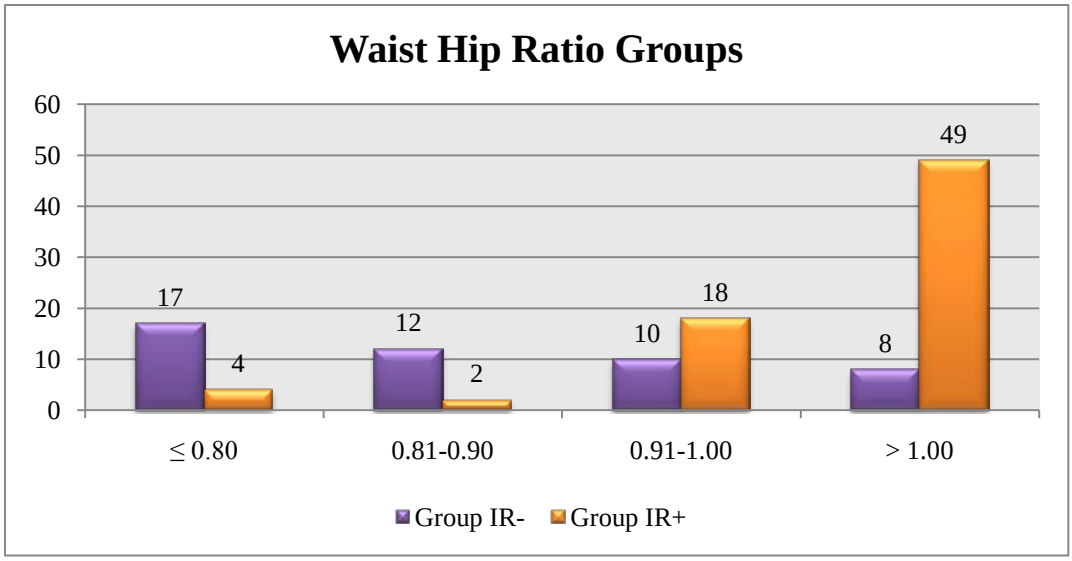


Waist Circumference Groups	Group IR-	%	Group IR+	%
≤ 90 cms	2	4.26	1	1.37
91-100 cms	43	91.49	13	17.81
101-110 cms	2	4.26	59	80.82
Total	47	100.00	73	100.00

Waist Circumference Distribution	Group IR-	Group IR+	P value Unpaired t Test
Mean	95.31	102.87	<0.0001
SD	3.29	3.60	

Majority of the study subjects in IR -ve group are distributed in 90-100 cms waist circumference group (n=43, 91.49%) and 101-110 cms waist circumference group in IR +ve group (n=59, 80.82%) (p= <0.0001, unpaired t test) , thereby showing a statistical significance.

WAIST HIP RATIO VS INSULIN RESISTANCE

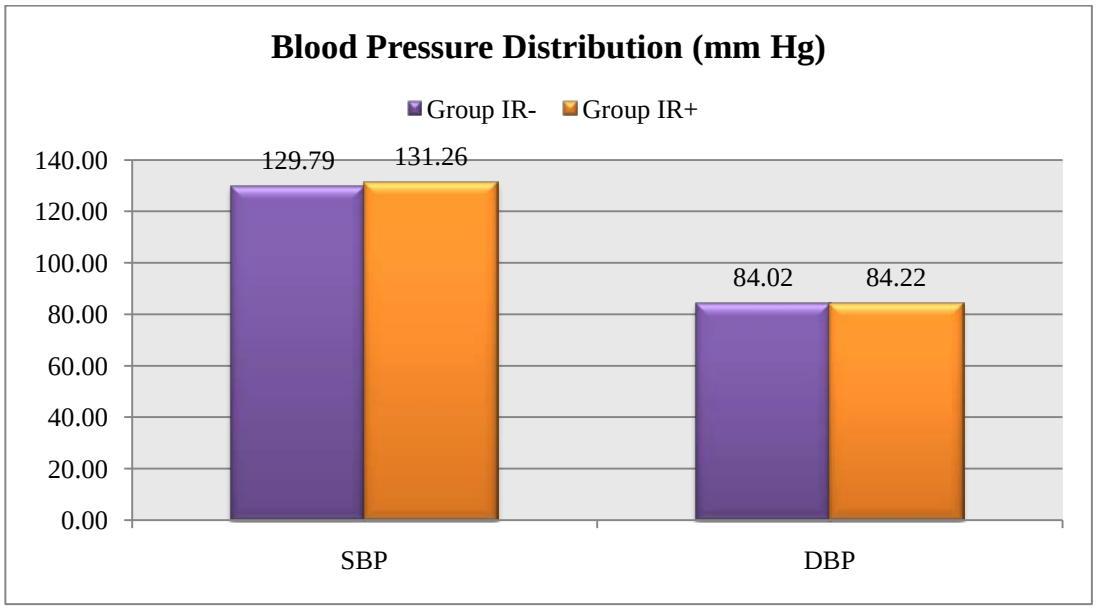


Waist Hip Ratio Groups	Group IR-	%	Group IR+	%
≤ 0.80	17	36.17	4	5.48
0.81-0.90	12	25.53	2	2.74
0.91-1.00	10	21.28	18	24.66
> 1.00	8	17.02	49	67.12
Total	47	100.00	73	100.00

Waist Hip Ratio Distribution	Group IR-	Group IR+	P value Unpaired t Test
Mean	0.89	1.02	<0.0001
SD	0.18	0.14	

Majority of the study subjects in IR -ve group are distributed in ≤ 0.80 waist hip ratio group (n=17, 36.17%) and > 1.00 waist circumference group in IR +ve group (n=49, 67.12%) (p= <0.0001, unpaired t test), thereby showing a statistical significance.

BLOOD PRESSURE VS INSULIN RESISTANCE



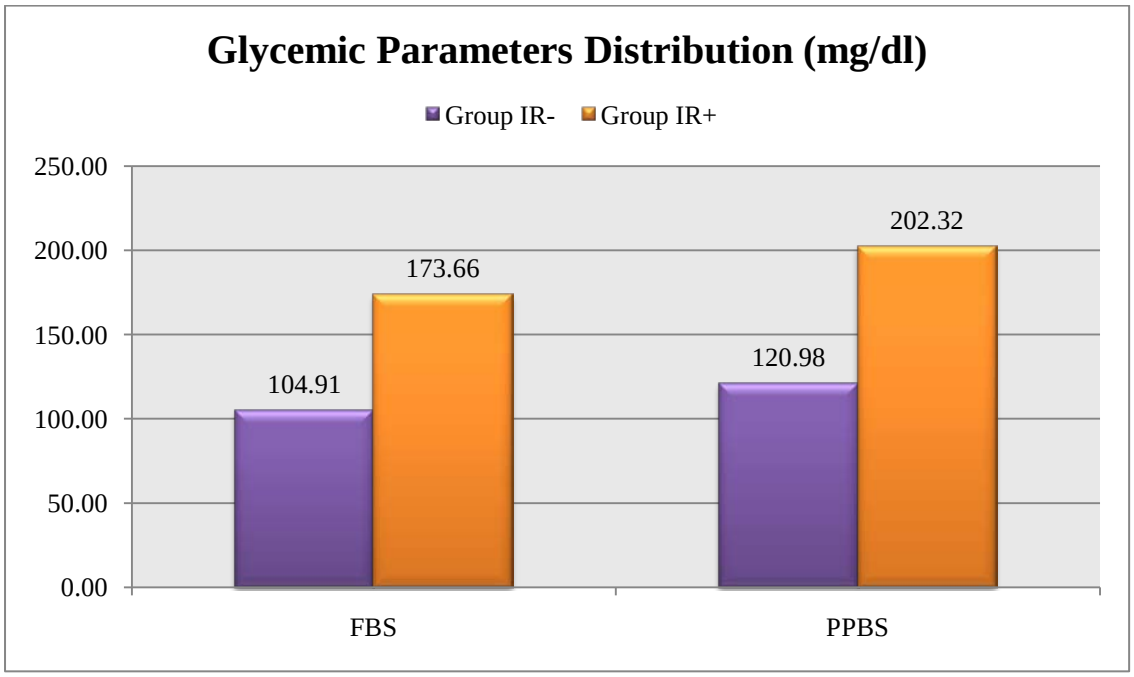
Blood Pressure Distribution (mm Hg)		SBP	DBP
Group IR-	Mean	129.79	84.02
	SD	10.13	5.66
Group IR+	Mean	131.26	84.22
	SD	11.18	6.03
P value Unpaired t Test		0.4665	0.8577

The mean SBP values are 129.79 mm Hg in IR -ve group and 131.26 mm Hg in IR +ve group (p=0.4665, unpaired t test)

The mean DBP values are 84.02 mm Hg in IR -ve group and 84.22 mm Hg in IR +ve group (p=0.8577, unpaired t test).

No statistical significance is achieved with regards to blood pressure.

GLYCEMIC PARAMETER DISTRIBUTION



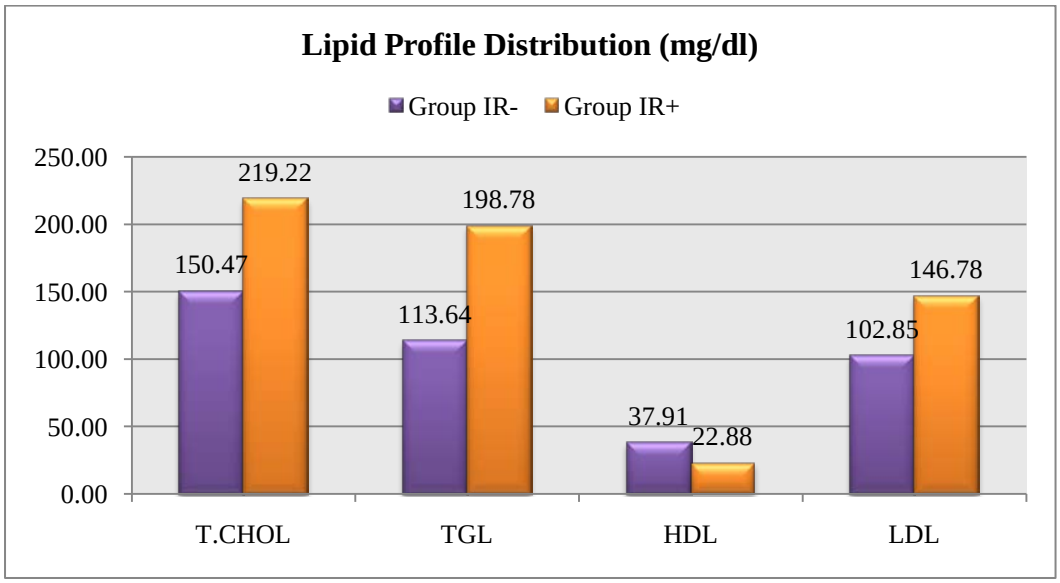
Glycemic Parameters Distribution (mg/dl)		FBS	PPBS
Group IR-	Mean	104.91	120.98
	SD	32.41	33.34
Group IR+	Mean	173.66	202.32
	SD	55.06	66.69
P value Unpaired t Test		<0.0001	<0.0001

The mean FBS values are 104.91 mg/dl in IR -ve group and 173.66 mg/dl in IR +ve group ($p < 0.0001$, unpaired t test)

The mean PPBS values are 120.98 mg/dl in IR -ve group and 202.32 mg/dl in IR +ve group ($p < 0.0001$, unpaired t test).

Hence there is significant statistical association.

LIPID ABNORMALITIES IN INSULIN RESISTANCE



Lipid Profile Distribution (mg/dl)		T.CHOL	TGL	HDL	LDL
Group IR-	Mean	150.47	113.64	37.91	102.85
	SD	14.48	43.93	7.73	14.95
Group IR+	Mean	219.22	198.78	22.88	146.78
	SD	28.69	76.74	6.70	16.93
P value Unpaired t Test		<0.0001	<0.0001	<0.0001	<0.0001

The mean cholesterol values are 150.47 mg/dl in IR -ve group and 219.22 mg/dl in IR +ve group (p <0.0001, unpaired t test)

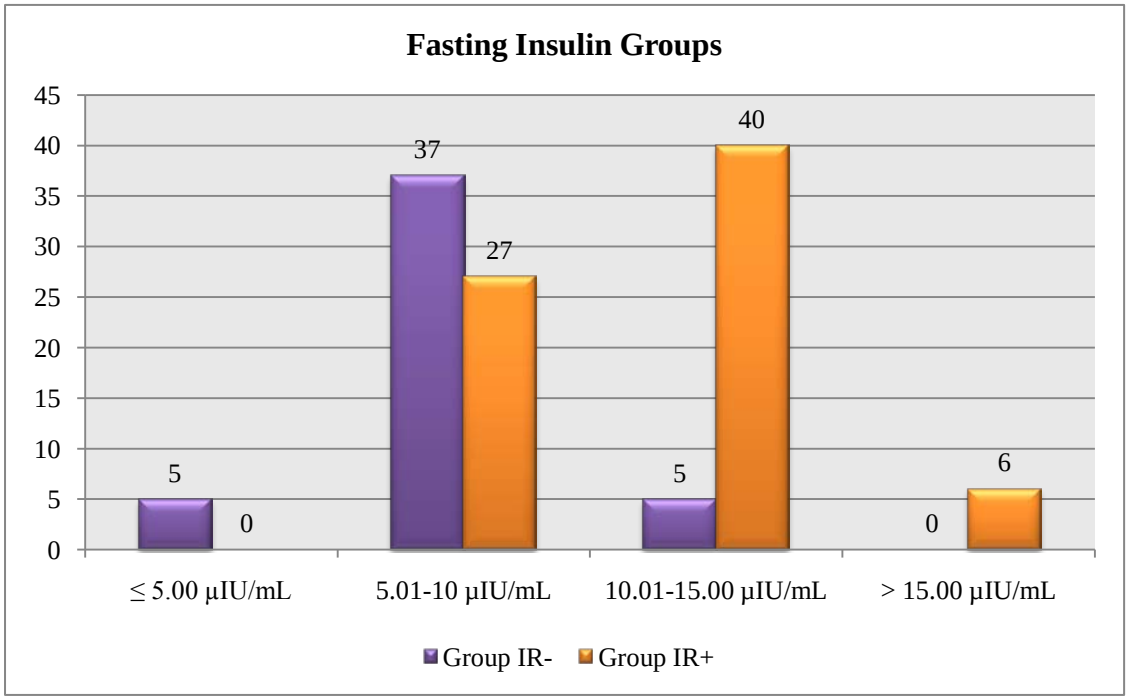
The mean TGL values are 113.64 mg/dl in IR -ve group and 198.76 mg/dl in IR +ve group (p <0.0001, unpaired t test)

The mean HDL values are 37.91 mg/dl in IR -ve group and 22.88 mg/dl in IR +ve group (p <0.0001, unpaired t test)

The mean LDL values are 102.85 mg/dl in IR -ve group and 146.78 mg/dl in IR +ve group (p <0.0001, unpaired t test).

Lipid parameters on analyzing gave a statistical significance.

FASTING INSULIN VS INSULIN RESISTANCE



Fasting Insulin Groups	Group IR-	%	Group IR+	%
≤ 5.00 µIU/mL	5	10.64	0	0.00
5.01-10 µIU/mL	37	78.72	27	36.99
10.01-15.00 µIU/mL	5	10.64	40	54.79
> 15.00 µIU/mL	0	0.00	6	8.22
Total	47	100.00	73	100.00

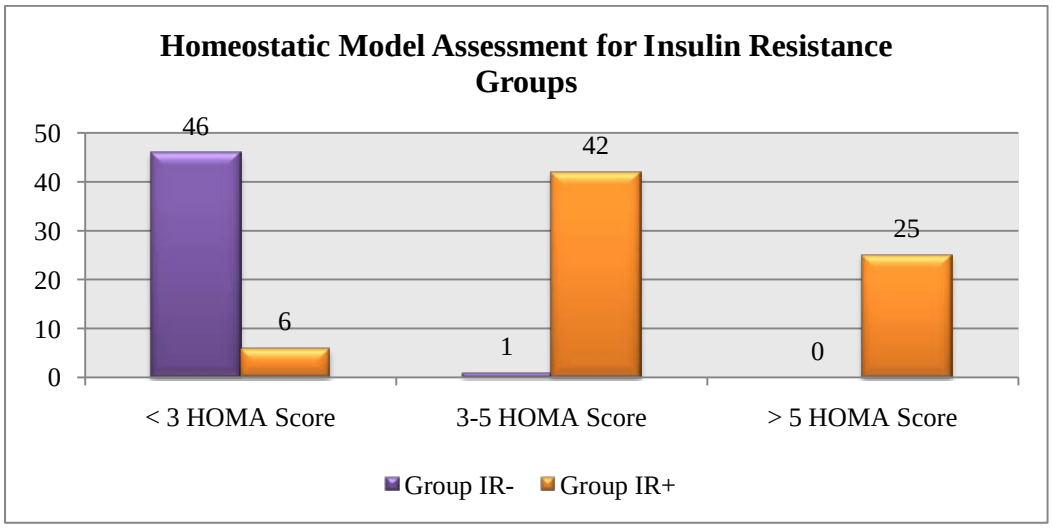
Fasting Insulin Distribution (µIU/mL)	Group IR-	Group IR+	P value Unpaired t Test
Mean	7.64	11.17	<0.0001
SD	1.91	2.75	

Majority of the study subjects in IR -ve group are distributed in 5.01-10 µIU/mL fasting insulin group (n=37, 78.72%) and 10.01-15.00 µIU/mL fasting insulin group in IR +ve group (n=40, 54.79%) (p= <0.0001, unpaired t test), thereby showing statistical significance .

HOMA IR vs INSULIN RESISTANCE

HOMA IR is calculated using the formula

$$\frac{\text{fasting insulin (}\mu\text{U/ml) x fasting glucose(mg/dl)}}{405}$$

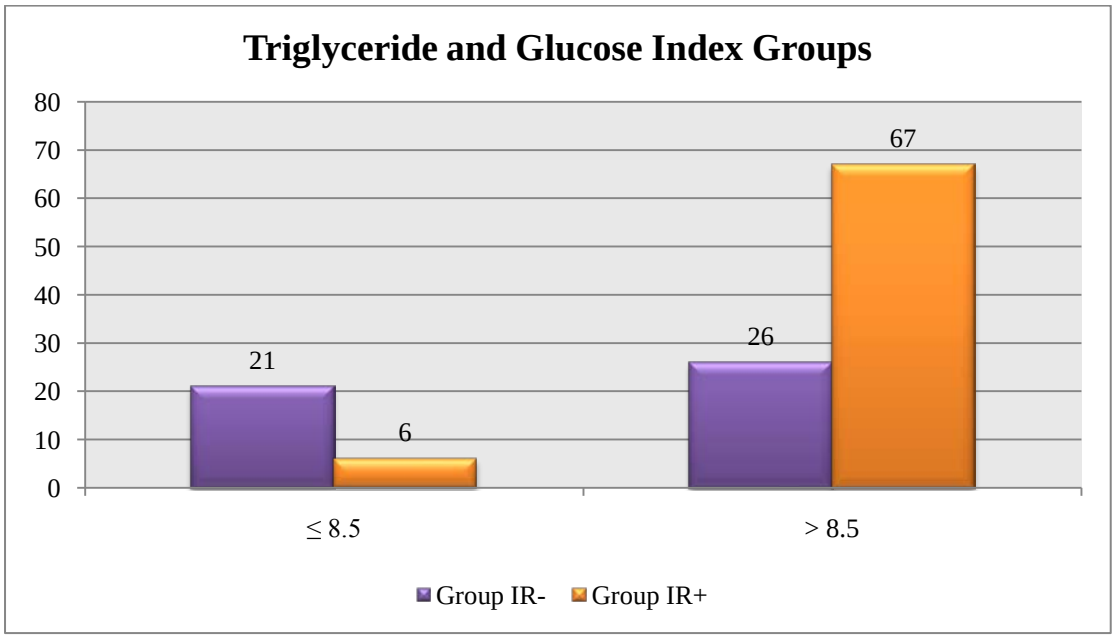


Homeostatic Model Assessment for Insulin Resistance Groups	Group IR-	%	Group IR+	%
< 3 HOMA Score	46	97.87	6	8.22
3-5 HOMA Score	1	2.13	42	57.53
> 5 HOMA Score	0	0.00	25	34.25
Total	47	100.00	73	100.00

Homeostatic Model Assessment for Insulin Resistance Distribution (mg/dl)	Group IR-	Group IR+	P value Unpaired t Test
Mean	1.83	4.55	<0.0001
SD	0.42	1.05	

Majority of the study subjects in IR -ve group are distributed < 3 HOMA Score group (n=46, 97.87%) and 3-5 HOMA Score group in IR +ve group (n=42, 57.53%) (p= <0.0001, unpaired t test), thereby giving a statistical significance.

TRIGLYCERIDE GLUCOSE INDEX VS INSULIN RESISTANCE

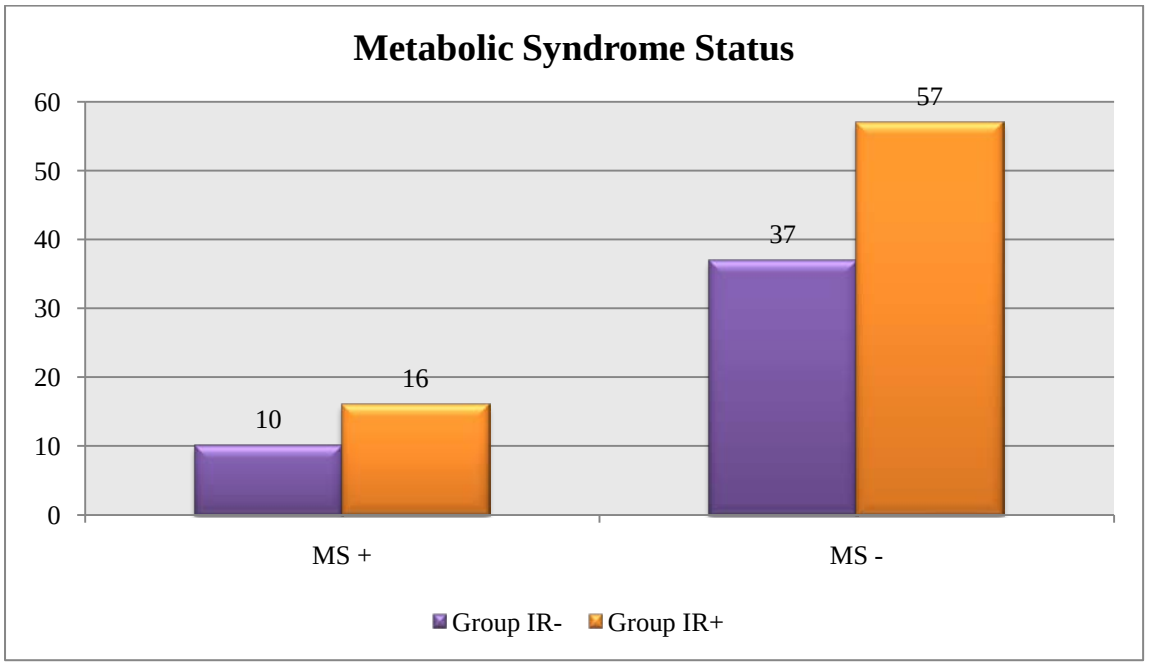


Triglyceride and Glucose Index Groups	Group IR-	%	Group IR+	%
≤ 8.5	21	44.68	6	8.22
> 8.5	26	55.32	67	91.78
Total	47	100.00	73	100.00

Triglyceride and Glucose Index Distribution	Group IR-	Group IR+	P value Unpaired t Test
Mean	8.66	9.64	<0.0001
SD	0.54	0.62	

Majority of the study subjects in IR -ve group are distributed > 8.5 triglyceride and glucose index group (n=26, 55.32%) and same group in IR +ve group (n=67, 91.78%) (p <0.0001, unpaired t test), having good statistical significance .

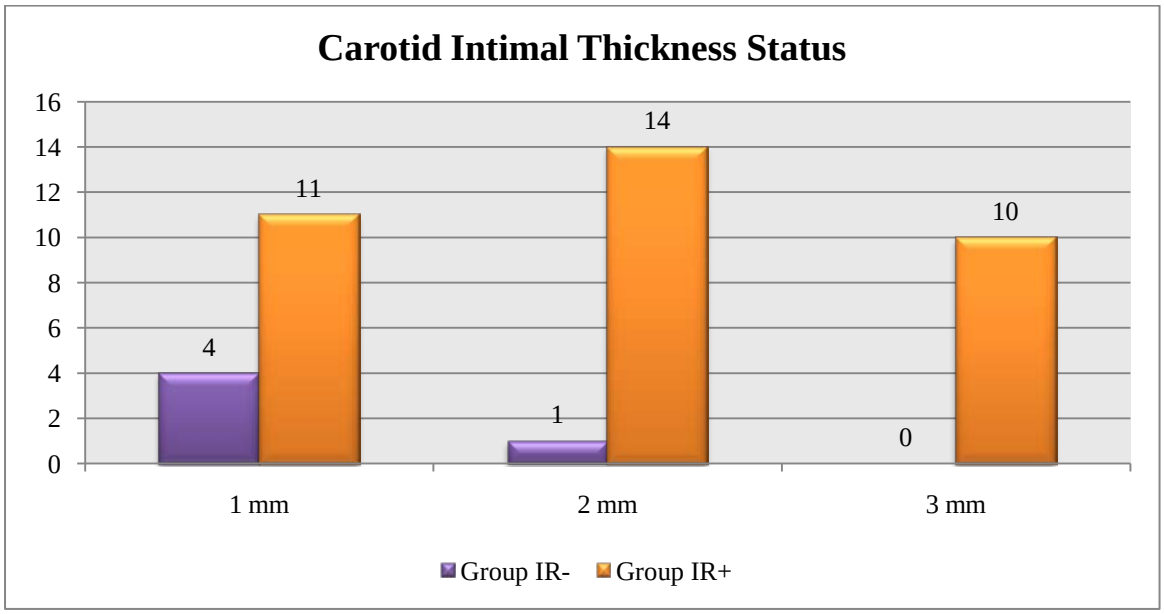
METABOLIC SYNDROME VS INSULIN RESISTANCE



Metabolic Syndrome Status	Group IR-	%	Group IR+	%	P value Chi Squared Test
MS +	10	21.28	16	21.92	0.9337
MS -	37	78.72	57	78.08	
Total	47	100.00	73	100.00	

Majority of the study subjects in IR -ve group are diagnosed as no metabolic syndrome (n=37, 78.72%) and same too in IR +ve group (n=57, 78.08%) (p=0.9337, chi squared test). No statistical significance is achieved with regards to metabolic syndrome.

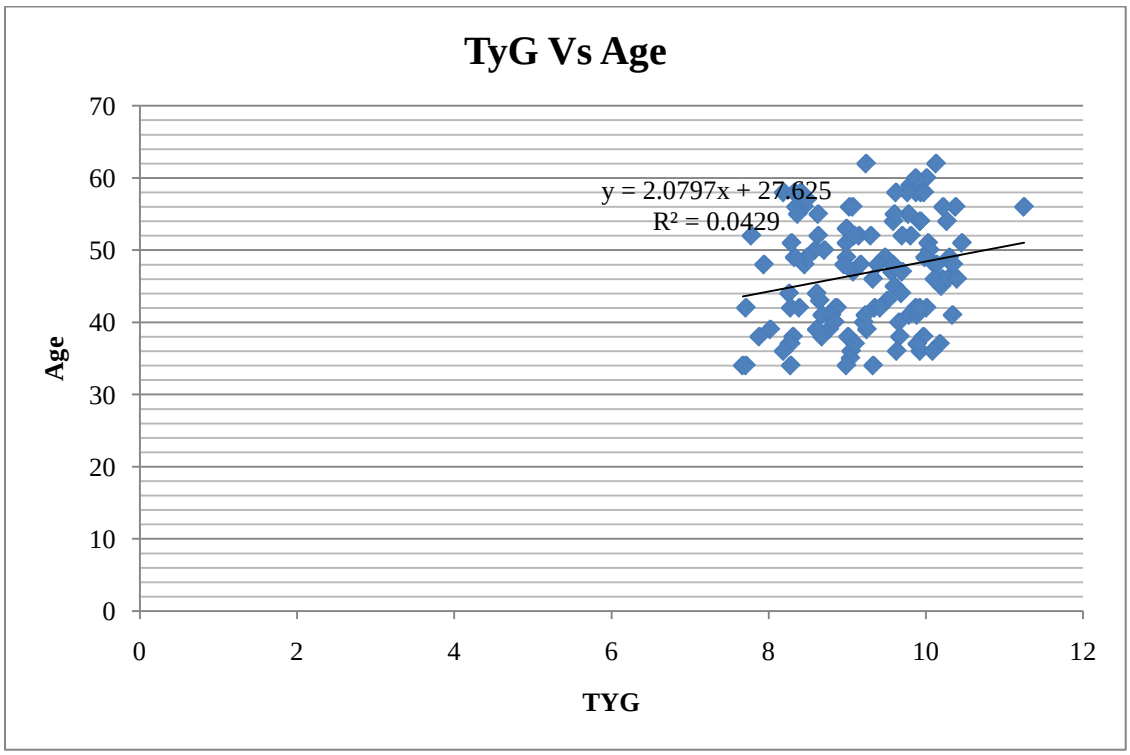
CAROTID INTIMAL THICKNESS VS INSULIN RESISTANCE



Carotid Intimal Thickness Status	Group IR-	%	Group IR+	%	P value Fishers Exact Test
1 mm	4	80.00	11	31.43	0.1083
2 mm	1	20.00	14	40.00	
3 mm	0	0.00	10	28.57	
Total	5	100.00	35	100.00	

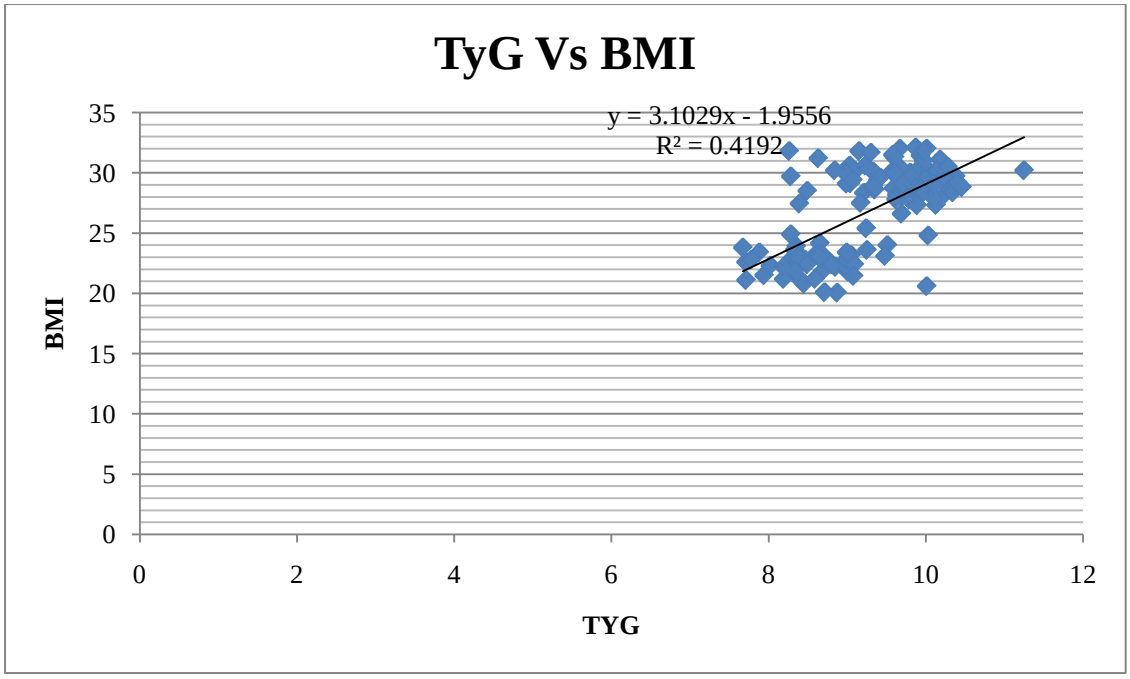
Majority of the study subjects in IR -ve group have carotid intimal thickness of 1 cm (n=4, 80%) and carotid intimal thickness of 2 cm too in IR +ve group (n=14, 40%) (p=0.1083, chi squared test), thereby no statistical significance is achieved.

CORRELATION



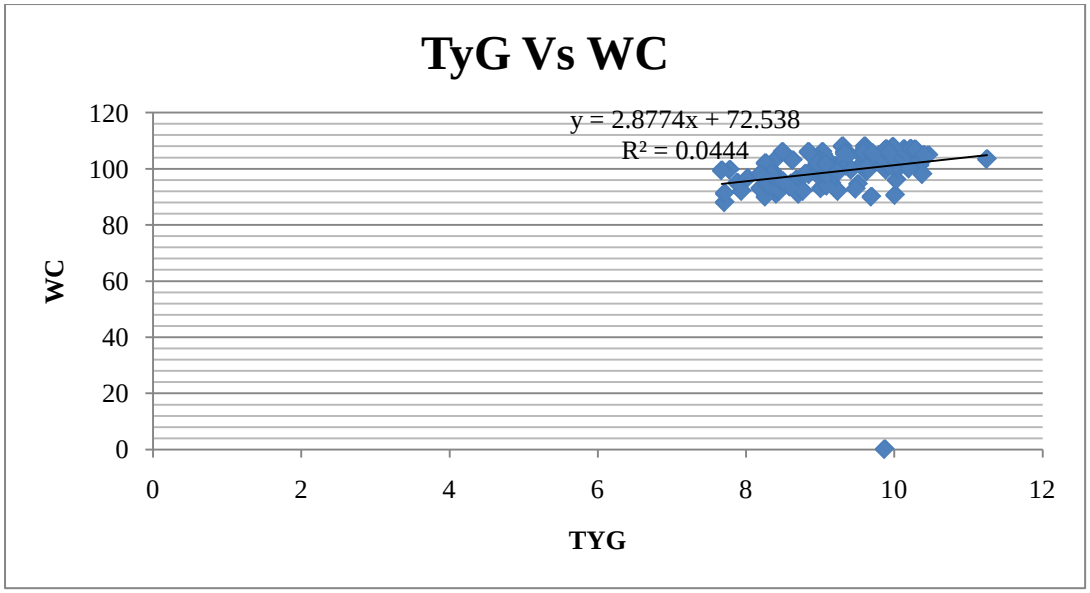
Regression Statistics - TyG Vs Age	
Pearson's R	0.21
R Square	0.04
P value ANOVA	0.0232

There is a positive correlation between TyG levels and age. This is indicated by the Pearson's R Correlation value of 0.21 with a poor statistical significance with a p-value of 0.0232.



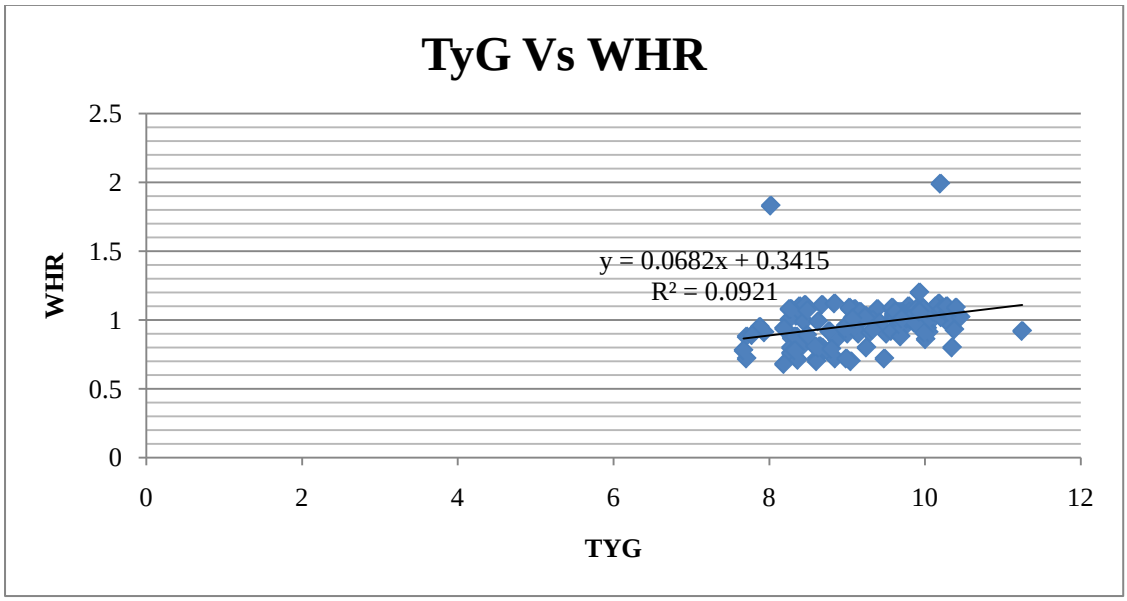
Regression Statistics - TyG Vs BMI	
Pearson's R	0.65
R Square	0.42
P value ANOVA	<0.0001

There is a positive correlation between TYG levels and BMI. This is indicated by the Pearson's R Correlation value of 0.65 and a statistically significant p-value of <0.0001.



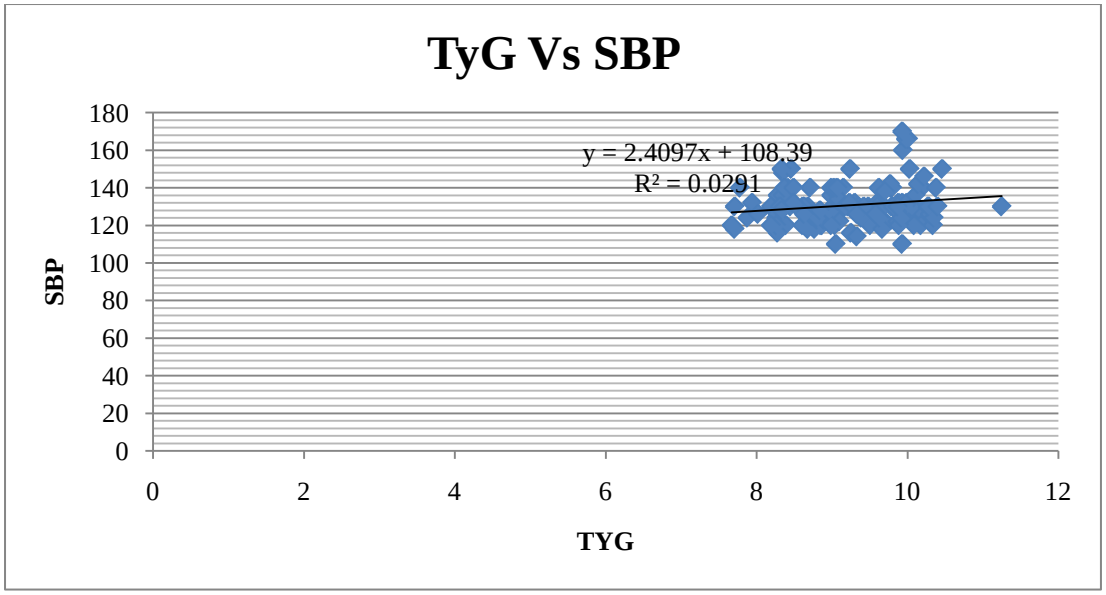
Regression Statistics - TyG Vs WC	
Pearson's R	0.21
R Square	0.04
P value ANOVA	0.0208

There is a positive correlation between TYG levels and waist circumference. This is indicated by the Pearson's R Correlation value of 0.21 statistically insignificant with a p value of 0.0208.



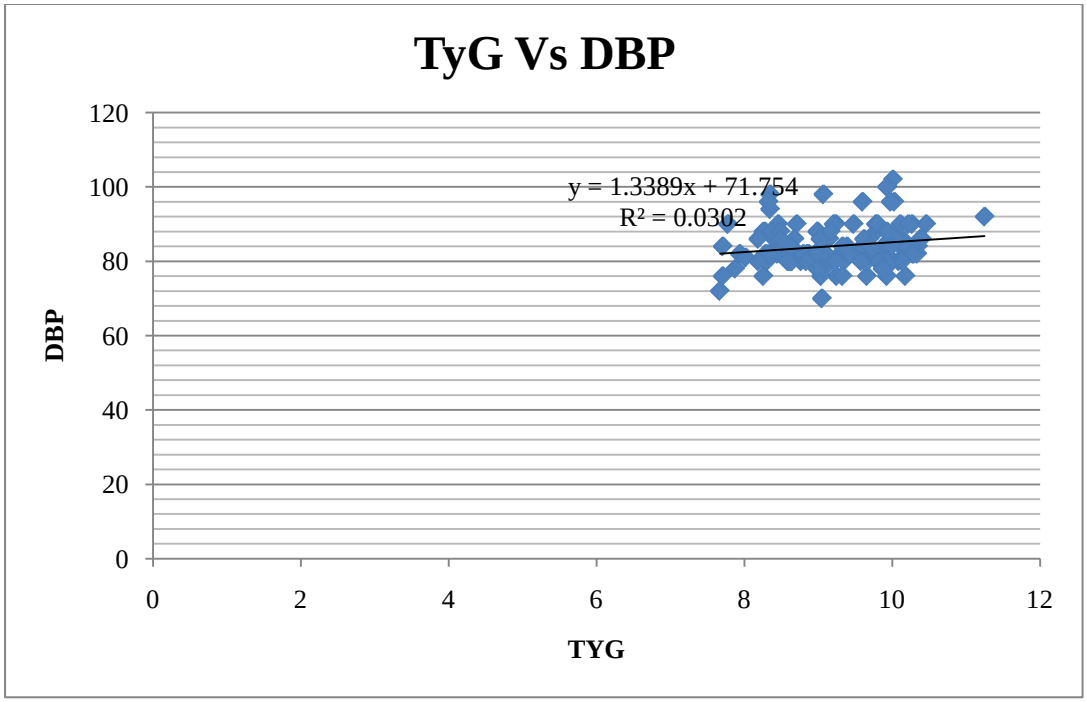
Regression Statistics - TyG Vs WHR	
Pearson's R	0.30
R Square	0.09
P value ANOVA	0.0007

There is a positive correlation between TyG levels and waist hip ratio. This is indicated by the Pearson's R Correlation value of 0.30 and a statistically significant p value of 0.0007 .



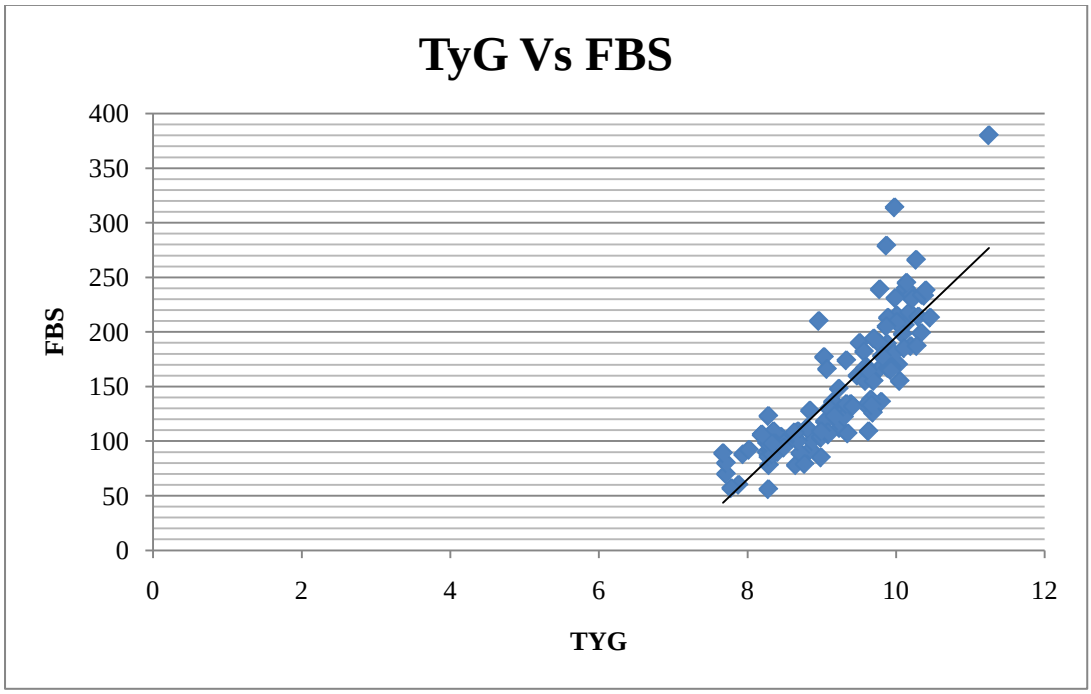
Regression Statistics - TyG Vs SBP	
Pearson's R	0.17
R Square	0.03
P value **ANOVA**	0.0625

There is a positive correlation between TyG levels and SBP. This is indicated by the Pearson's R Correlation value of 0.30 and a statistical significance with p value of 0.0625 .



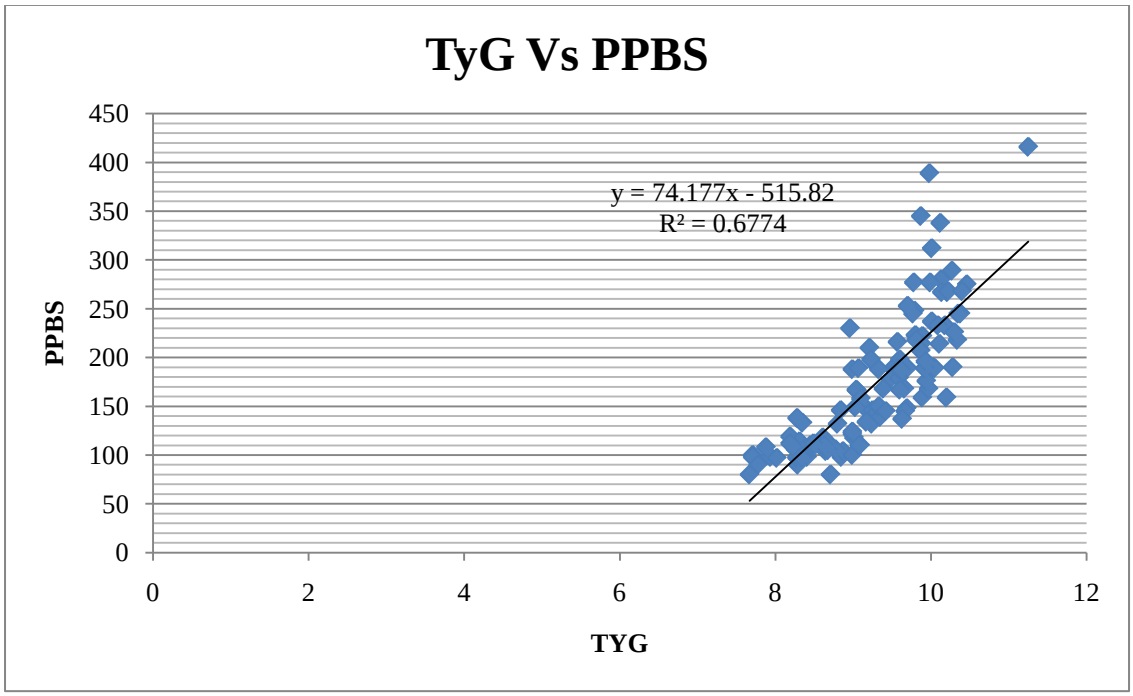
Regression Statistics - TyG Vs DBP	
Pearson's R	0.17
R Square	0.03
P value **ANOVA**	0.0576

There is a positive correlation between TYG levels and DBP. This is indicated by the Pearson's R Correlation value of 0.30 and statistical insignificance with p value 0.0576.



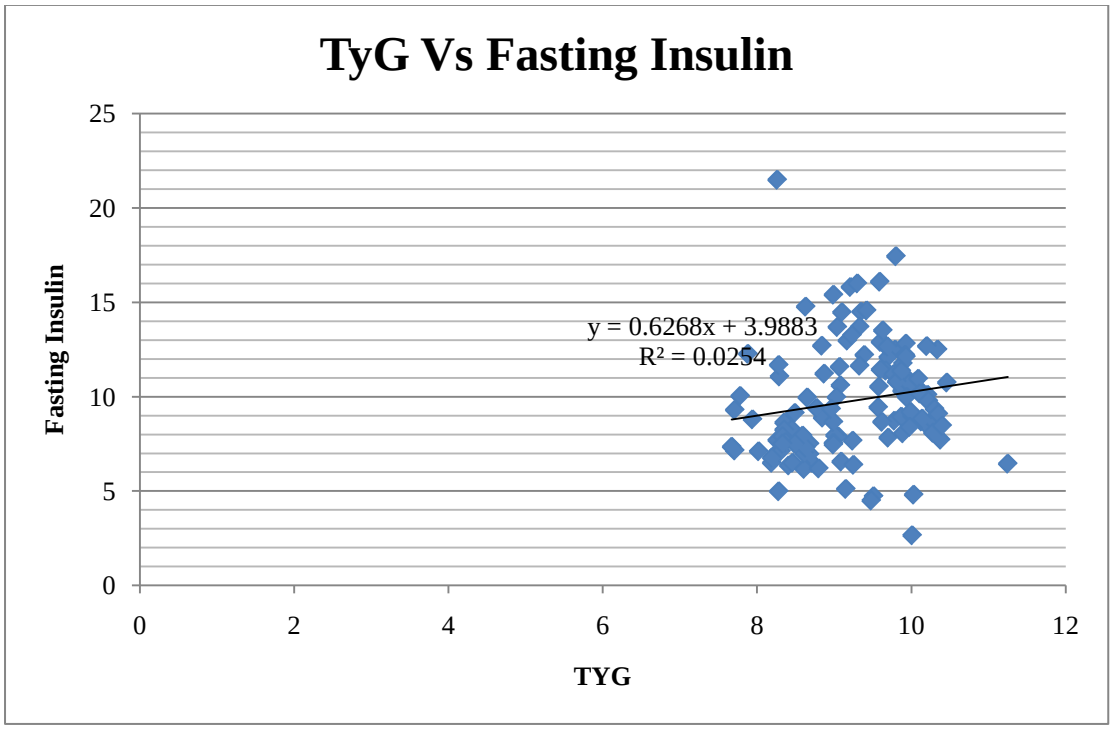
Regression Statistics - TyG Vs FBS	
Pearson's R	0.85
R Square	0.73
P value ANOVA	<0.0001

There is a positive correlation between TyG levels and FBS. This is indicated by the Pearson's R Correlation value of 0.85 with a p-value of <0.0001. Hence it had a statistically significant correlation .



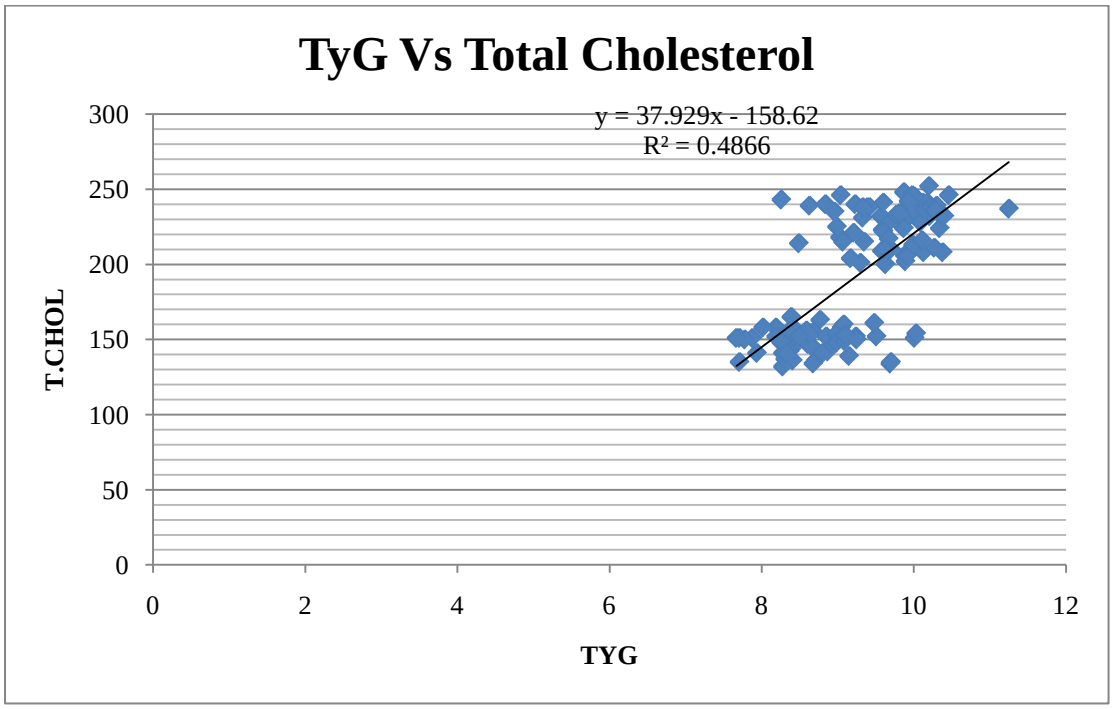
Regression Statistics - TyG Vs PPBS	
Pearson's R	0.82
R Square	0.68
P value **ANOVA**	<0.0001

There is a positive correlation between TyG levels and PPBS. This is indicated by the Pearson's R Correlation value of 0.82 and a statistically significant p value of 0.0001.



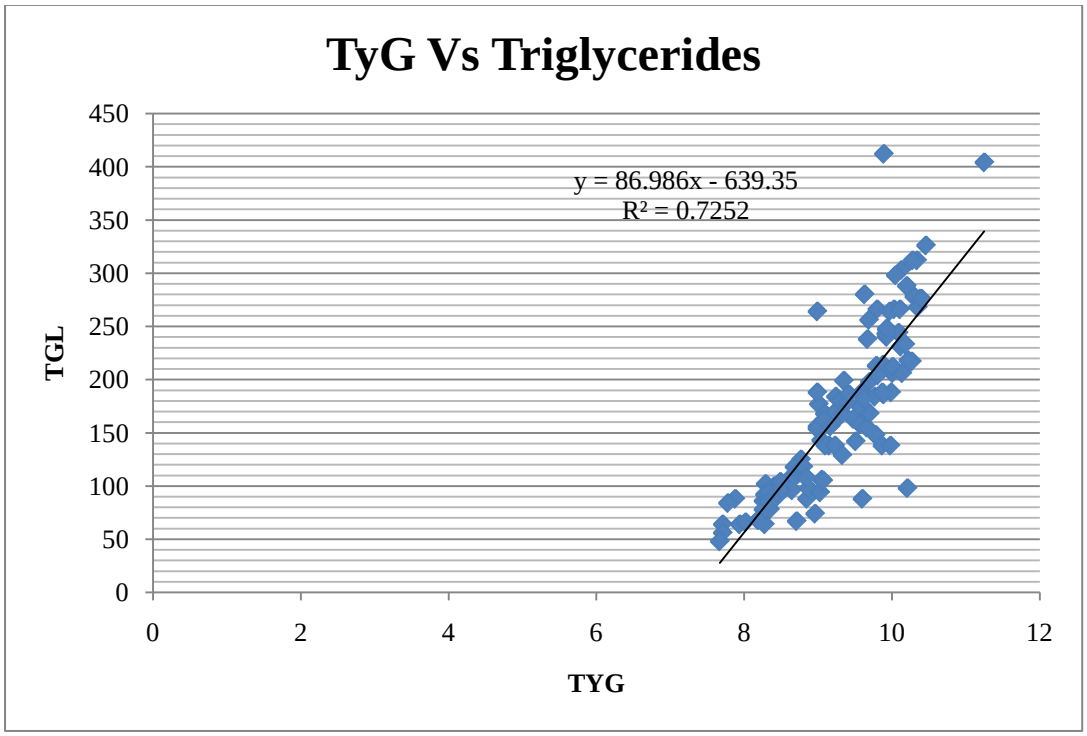
Regression Statistics - TyG Vs Fasting insulin	
Pearson's R	0.16
R Square	0.03
P value **ANOVA**	0.0822

There is a positive correlation between TyG levels and fasting insulin. This is indicated by the Pearson's R Correlation value of 0.36 and a statistical insignificance with p value of 0.0822 is arrived.



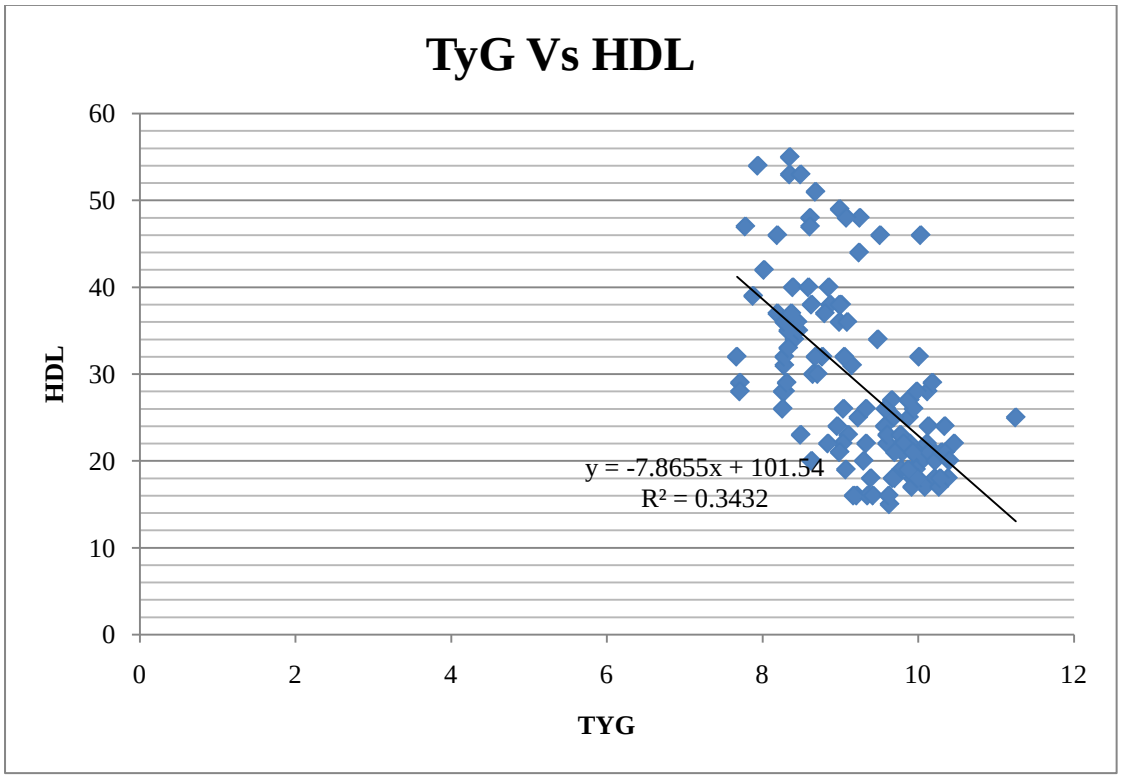
Regression Statistics - TyG Vs Total cholesterol	
Pearson's R	0.70
R Square	0.49
P value **ANOVA**	<0.0001

There is a positive correlation between TYG levels and TC. This is indicated by the Pearson's R Correlation value of 0.70 and a statistical significant correlation with a p value of less than 0.0001.



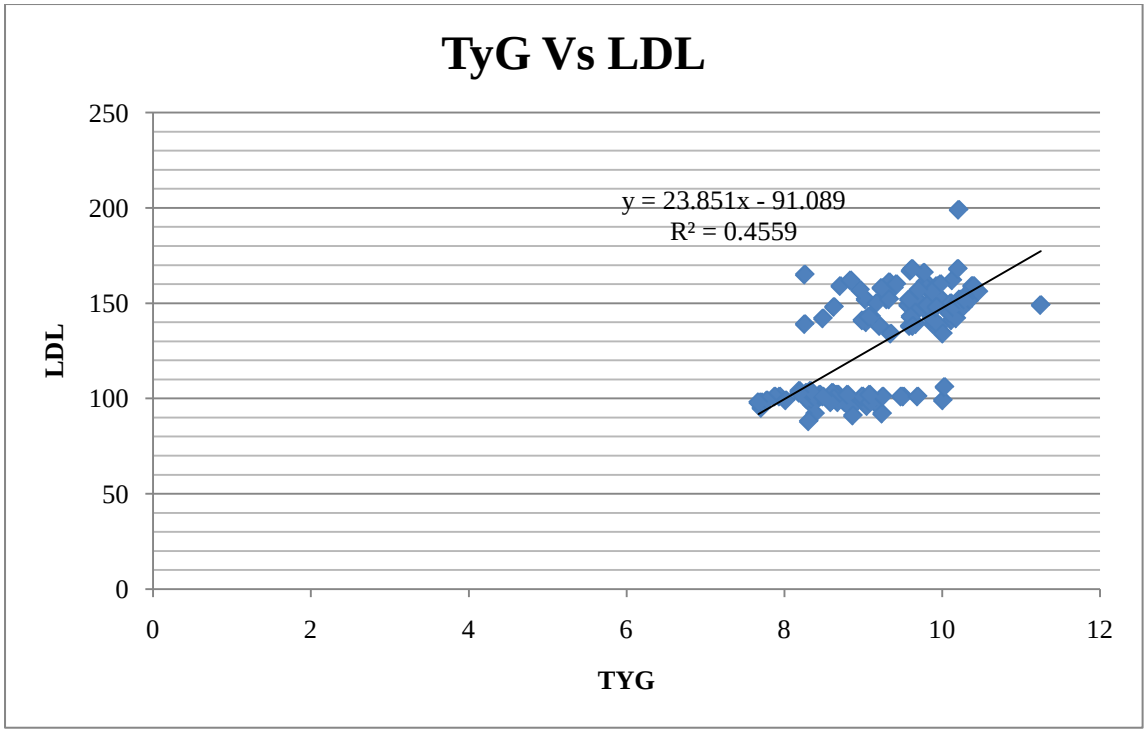
Regression Statistics - TyG Vs Triglycerides	
Pearson's R	0.85
R Square	0.73
P value **ANOVA**	<0.0001

There is a positive correlation between TyG levels and TG. This is indicated by the Pearson's R Correlation value of 0.85 and a statistically significant correlation with a p value of less than 0.0001.



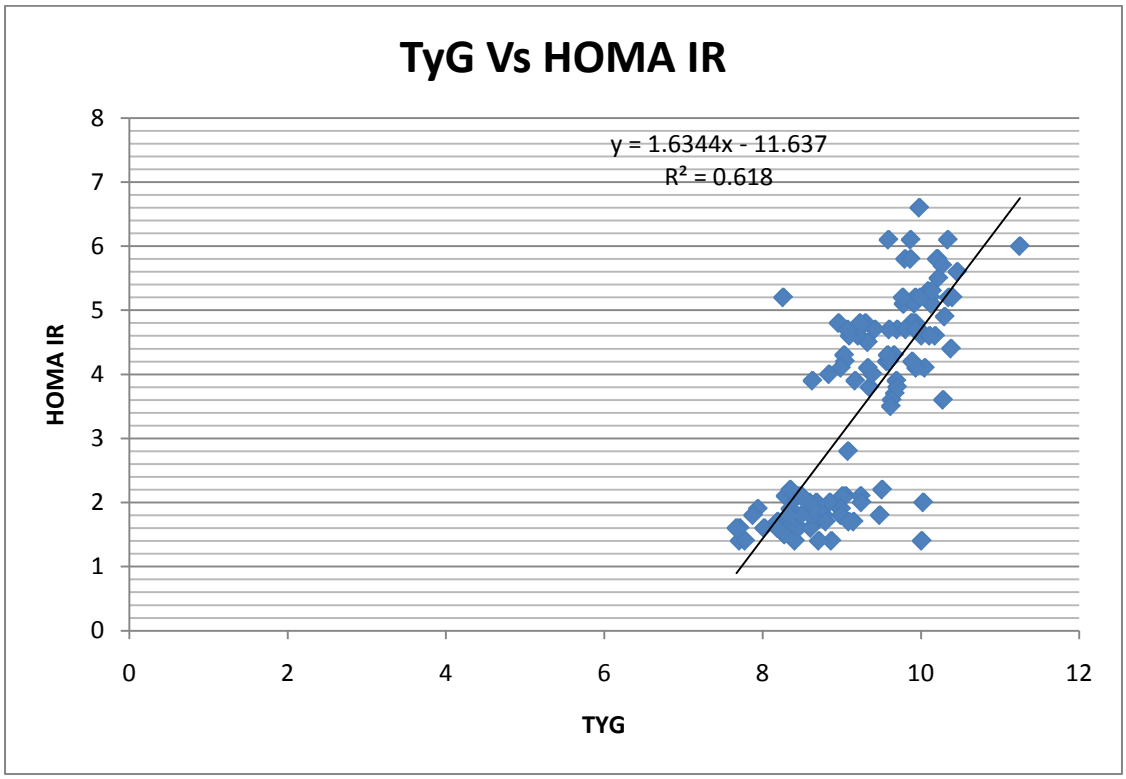
Regression Statistics - TyG Vs HDL	
Pearson's R	-0.59
R Square	0.34
P value ANOVA	<0.0001

There is a negative correlation between TYG levels and HDL. This is indicated by the Pearson's R Correlation value of -0.59 and a statistically significant correlation with a p value of less than 0.0001.



Regression Statistics - TyG Vs LDL	
Pearson's R	0.68
R Square	0.46
P value **ANOVA**	<0.0001

There is a positive correlation between TyG levels and LDL. This is indicated by the Pearson's R Correlation value of 0.68 and a statistically significant correlation with p value of less than 0.0001.



Regression Statistics - TyG Vs HOMA IR	
Pearson's R	0.79
R Square	0.79
P value **ANOVA**	<0.0001

There is a positive correlation between TyG levels and HOMA score. This is indicated by the Pearson's R Correlation value of 0.79 and a statistically significant correlation with a p value of less than 0.0001.

Accuracy Analysis - DM

Accuracy Analysis	Cut Off	Sensitivity	Specificity	PPV	NPV	LR +	LR -	AUC	P value
TyG	8.65	0.84	0.83	0.64	0.93	4.87	0.19	0.900	<0.0001
HOMA IR	3.54	0.79	0.69	0.48	0.90	2.57	0.30	0.855	<0.0001

TyG INDEX

Sensitivity

- Sensitivity of TyG is high, meaning that 84% of those with DM will have a positive test result with TyG

Specificity

- Specificity of TyG is high, meaning that 83% of those without DM will have a negative test result with TyG

Positive Predictive Value

- Positive predictive value of TyG is high, meaning 64% of individuals with positive TyG test will actually have DM

Negative Predictive Value

- Negative predictive value of TyG is high, meaning 93% of individuals with negative TyG test will actually not have DM

HOMA IR

Sensitivity

- Sensitivity of HOMA IR is high, meaning that 79% of those with DM will have a positive test result with HOMA IR

Specificity

- Specificity of HOMA IR is high, meaning that 69% of those without DM will have a negative test result with HOMA IR

Positive Predictive Value

- Positive predictive value of HOMA IR is high, meaning 48% of individuals with positive HOMA IR test will actually have DM

Negative Predictive Value

- Negative predictive value of HOMA IR is high, meaning 90% of of individuals with negative HOMA IR test will actually not have DM

DISCUSSION

The prime intention of this study is to test whether the novel and simple marker of insulin resistance (i.e) TyG-Index, associates with the presence of carotid atherosclerosis, and other metabolic and anthropometric parameters and above all its efficiency when compared with the classic HOMA IR which is being used for insulin resistance estimation in a wide basis.

- In our study conducted in a population of 120 at Kilpauk medical college, between the study groups (people with insulin resistance (47) and without insulin resistance(73) who came for diabetes screening), with regards to age and gender the difference in the mean age of patients in IR-ve group (46.26) and IR +ve group (47.26) was found to be statistically insignificant (p value 0.4844). Also, the difference in the percentages of males in IR -ve group and IR +ve group (2.04) was found to be statistically insignificant (p value 0.8249). This relates with a previous study done in a Italian population by Giovanni cuda et al [117] which stated that there is no statistical significance to TyG index with regards to age and gender. This study also brought a interesting finding that TyG index gradually increased with age in those with normal glycemia and with fasting glucose in the range 101–125 mg/dl, while there

was a slow but progressive decrease in individuals with glycaemia of >125 mg/dl.

- Among anthropometric measurements, mean BMI of patients in IR -ve group (23.21) and IR +ve group (29.03) was found to be statistically significant (p <0.0001). Infact, the decreased difference in mean BMI in IR -ve group compared to IR +ve group was 6.82 points, showing a 20% lowering.

- The difference in the mean WC of patients in IR -ve group (95.31) and IR +ve group (102.87) was found to be statistically significant (p <0.0001). The decreased difference in mean waist circumference in IR -ve group compared to IR +ve group was 7.56 points, showing a 7% lowering, showing that WC had independent positive association with insulin resistance . The difference in the mean waist hip ratio of patients in IR -ve group (0.89) and IR +ve group (1.02) was found to be statistically significant (p <0.0001). The decreased difference in mean waist hip ratio in IR -ve group compared to IR +ve group was 0.13 points, showing a 13% reduction, establishing a independent positive association with insulin resistance.

- Blood pressure distribution between the study groups, the difference in the mean SBP and DBP of patients in IR -ve group

and IR +ve group (1.47 and 0.20) was found to be statistically insignificant (p >0.05). FBS and PPBS of patients in IR -ve group and IR +ve group (68.74 and 81.34) was found to be statistically significant (p value 0.4665, 0.8571 respectively), showing a independent positive association with insulin resistance.

- During the process of statistically analyzing lipid parameters distribution between the study groups, the difference in the mean cholesterol of patients between IR -ve group and IR +ve group (68.75) was found to be statistically significant (p <0.0001) showing a 31% lowering.

- The difference in the mean TGL of patients between IR -ve group and IR +ve group (85.14) was found to be statistically significant (p <0.0001) showing a 43% lowering.

- The difference in the mean HDL of patients between IR -ve group and IR +ve group (15.04) was found to be statistically significant (p <0.0001) showing a 40% elevation.

- The difference in the mean HDL of patients between IR -ve group and IR +ve group (43.93) was found to be statistically significant (p <0.0001) showing a 30% lowering , establishing that

cholesterol, TGL, HDL and LDL has a independent positive association with insulin resistance.

- These findings were consistent with yet another study done by Tingting du et al [118] in a set of Chinese population which brought out similar results (significant statistical association of lipid parameters and TyG index). However it also brought out an interesting fact that models with lipid ratios were consistently superior to lipid variables used alone for prediction.

- The difference in the percentages of metabolic syndrome patients in IR -ve group and IR +ve group (0.64) was found to be statistically insignificant ($p > 0.05$), the difference in the percentages of carotid intimal thickness in IR -ve group and IR +ve group was found to be statistically insignificant ($p = 0.1083$).

- With regards to fasting insulin, HOMA IR and TyG index, The difference in the mean fasting insulin of patients in IR -ve group (7.64) and IR +ve group (11.17) was found to be statistically significant ($p < 0.0001$). The decreased difference in mean fasting insulin in IR -ve group compared to IR +ve group was 3.53 points, showing a 32% lowering. the difference in the mean HOMA Score of patients in IR -ve group (1.83) and IR +ve group (4.55) was found to be statistically significant ($p < 0.0001$). The decreased

difference in mean HOMA Score in IR -ve group compared to IR +ve group was 2.72 points, showing a 60% lowering, establishing a positive association independently. The difference in the mean triglyceride and glucose index of patients in IR -ve group (8.66) and IR +ve group (9.84) was found to be statistically significant ($p < 0.0001$). The decreased difference in mean triglyceride and glucose index in IR -ve group compared to IR +ve group was 0.98 points, showing a 10% lowering.

TYGINDEX AND ITS CORRELATION

- TyG index had a statistically significant positive correlation with age, indicated by the Pearson's R Correlation value of 0.21 with a p-value of 0.0232. In simple terms, for every 27 years increase in age there is a 1 unit increase in TyG among the study subjects.
- As BMI increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 3 unit increase in BMI there is a 1 unit increase in TyG among the study subjects.
- Waist circumference increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 2.87 unit increase in waist circumference there is a 1 unit increase in TyG among the study subjects.
- Waist hip ratio increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 0.34 unit increase in waist hip ratio there is a 1 unit increase in TyG among the study subjects.
- The relationship between the TyG and SBP as well as DBP is considered to be statistically insignificant since $p > 0.05$.

- FBS increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 65.19 unit increase in FBS there is a 1 unit increase in TyG among the study subjects.

- PPBS increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 74.17 unit increase in PPBS there is a 1 unit increase in TyG among the study subjects.

- TC increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 37.93 unit increase in TC there is a 1 unit increase in TyG among the study subjects.

- The relationship between the TyG and TG is considered to be statistically significant since $p < 0.0001$. This means as TG increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 86.98 unit increase in TG there is a 1 unit increase in TyG among the study subjects.

- The relationship between the TyG and HDL is considered to be statistically significant since $p < 0.0001$. This means as HDL increases TyG also decreases in a direct and inverse fashion in our study subjects. In simple terms, for every 7.86 unit increase in HDL there is a 1 unit decrease in TGY among the study subjects.

- The relationship between the TyG and LDL is considered to be statistically significant since $p < 0.0001$. This means as LDL

increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 23.85 unit increase in LDL there is a 1 unit increase in TyG among the study subjects.

- HOMA score increases TyG also increases in a direct and linear fashion in our study subjects. In simple terms, for every 1.63 unit increase in HOMA score there is a 1 unit increase in TyG among the study subjects.

The diagnostic effectiveness or diagnostic accuracy in relation to TyG test is an excellent case finding or diagnostic test with high specificity and PPV suggesting that false positives are very rare. It is also a good screening test with high sensitivity and NPV suggesting that high false negative tests will occur rarely compared to HOMA IR.

- Our study is consistent with the findings of another study done by Irace et al [119] conducted in an Italian cohort which proved that TyG index is better compared to HOMA IR in assessing insulin resistance.

- Our study also have got a consistency with a similar study done in a argentinal cohort by Giselaunger et al [120] which first came up with the proof that TyG index is a good discriminant of metabolic syndrome .

CONCLUSION

- The simplicity and low cost biochemical measurements warrant further investigation of the role of TyG index as a surrogate marker of IR to identify individuals at risk of cardiometabolic risk and facilitate the prevention of chronic disease associated with IR.
- In our study conducted in 120 patients, in Kilpauk Medical College, the efficiency of TyG index in assessing insulin resistance in newly detected diabetics was carried out in comparison to HOMA IR.
- TyG index established a positive correlation with almost all anthropometric and Metabolic Parameters. There was a statistically significant correlation with a p value of less than 0.0001 between Age, BMI, waist circumference, WHR, fasting and postprandial blood sugars and all the lipid parameters. However, blood pressure (both systolic and diastolic) and carotid intimal thickness did not achieve significant correlations with these indices showed by p value of 0.8557, 0.9337 respectively.
- TyG index cutoff was calculated. Those with 8.65 were definitely diabetics. If these data are established in future observations, and in other populations, the TyG-Index could be converted in to a simple but effective tool for risk assessment in daily clinical practice.

- TyG index also gave a positive correlation with HOMA IR; Indeed , the ROC curve analysis showed that TyG index had the largest AUC, thus demonstrating its superior performance in recognizing IR than HOMAIR .

- Our study had few limitations. First, because of the crosssectional design, the associations were not prospective and causality cannot be inferred. Further longtitudinal study is necessary to confirm if TyG index may predict future occurrence of IR. Secondly, because the study includes south Indian individuals, the results cannot be generalized to other ethnicitie; As triglyceride levels varies according to ethnicity, further research is required to evaluate TyG index in different populations.

- All patients who are insulin resistant are advised to undergo strength training , endurance exercise (walking 5 days a week for about 30 minutes a day) and other aneorobic activities; avoidance of smoking and tobacco ; low carb , high protein diet is advised ; foods rich in omega 3 fatty acids are also encouraged; vitamin D and magnesium supplements are added along .All patients are advised to hold a follow up visit once a month for strict dietary and exercise adherence related education and tight medical checkup .

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PROFORMA

Patient's Name : Hospital Id No : Contact Number :

Age

Sex

Address

Native

Occupation

Sedentary / Non Sedentary

Socioeconomic Status

Food Habits ; Veg / Non Veg If Non Veg How Frequent ……Days / Week

Frequency Of Fast Foods / Junks In Aweek 2/3/4/>5

Recreational Habits : Sports / Gyming / Regular Walking, Jogging / Others

Cigarrette / Beedi / Hans / Alcohol / Snuff Powder / Tobbacco Chewing

Other Medications – Steroids / Antidiabetic Medications / Diuretics / Beta Blockers / Antipsychotics / Niacin Intake / Immunosuppresants, Others If Any ……??

Family H/O Diabets / Hypertension / Cad / Stroke / Tia/ Peripheral Vascular Disease / Pcos

Other Complaints If Any ?? ……..

Reason For Routine Screening If Any ? ……

PHYSICAL EXAMINATION

- Pallor/ Cyanosis / Clubbing / Jaundice / Pedal Dema / Generalised Lymphadenopathy
- Xanthoms / Xanthelesma / Earlobe Crease / Arcus / Skin Tags / Acanthosis Nigricans

ANTHROPOMETRIC MEASUREMENTS

Weight In Kgs …….

Height In Cms ……..

Calculated Bmi……..

Waist Circumference In Cms …….

Hip Circumference In Cms …….

Calculated Waist Hip Ratio ……

Neck Circumference In Cms …….

VITAL SIGNS :

Blood Pressure - / Mmhg

Pulse Rate - /Mt

Thickening Of Vessel Wall + / -

All Peripheral Pulses Felt Equally – Yes / No

Special Characters

Respiratory Rate –

Temperature –

SYSTEMIC EXAMINATION:

Cvs – S1s2 + / Carotid Bruit

Rs – Nvbs Heard / No Added Sounds

P/A – Soft ; Abdominal Obesity +/- ; Bruit Heard + / - ; Bs +/-

Cns – Nfnd At Present

சுயஒப்புதல் படிவம்

தலைப்பு:-
"உயர்மாவுசத்து கொழுப்பு சர்க்கரை குறியிட்டை உயிரின் இன்சுலின் எதிர்பாற்றல கண்டறியும் அளவிடாக பயன்படுத்தும் ஒரு ஆய்வு"

இடம்:

பொது மருத்துவத்துவ துர

அரசு கீழ்பாக்கம் மருத்துவ கல்லூரிமருத்துவமனை

சென்னை

பங்குபெறுபவரின் பெயர் :

பங்குபெறுபவரின் வயது : பங்குபெறுபவரின் எண் :

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள்எனக்கு விளக்கப்பட்டது. நான் இவ்வாய்வில்தன்னிச்சையாக பங்கேற்கிறேன். எந்த காரணத்தினாலோஎந்த சட்டசிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில்இருந்து விலகிக்கொள்ளல்லாம் என்றும் அறிந்துகொண்டேன்.

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும்ஆய்வு மேற்கொள்ளும்போதும் இந்த ஆய்வில்பங்கு பெறும்மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைபார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்துகொள்கிறேன். இந்த ஆய்வின் மூலம் கிடைக்கும்தகவலையோ, முடிவையோ பயன்படுத்திக்கொள்ள மறுக்கமாட்டேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்குஉண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன்.

பங்கேற்பவரின் கையொப்பம் ஆய்வாளரின் கையொப்பம்

இடம் :

தேதி :

PATIENT CONSENT FORM

STUDY DETAIL: **"TRIGLYCERIDE GLUCOSE INDEX AS A MARKER OF INSULIN RESISTANCE "**

STUDY CENTRE: KILPAUK MEDICALCOLLEGE, CHENNAI

PATIENTS NAME:

PATIENTS AGE:

IDENTIFICATION NUMBER :

PATIENT MAY CHECK ( ) THESE BOXES

☐ I CONFIRM THAT I HAVE UNDERSTOOD THE PURPOSE OF PROCEDURE FOR THE ABOVE STUDY. I HAVE THE OPPORTUNITY TO ASK QUESTION AND ALL MY QUESTIONS AND DOUBTS HAVE BEEN ANSWERED TO MY COMPLETE SATISFACTION.

☐ I UNDERSTAND THAT MY PARTICIPATION IN THE STUDY IS VOLUNTARY AND THAT I AM FREE TO WITHDRAW AT ANY TIME WITHOUT GIVING REASON, WITHOUT MY LEGAL RIGHTS BEING AFFECTED.

☐ I UNDERSTAND THAT SPONSOR OF THE CLINICAL STUDY, OTHERS WORKING ON THE SPONSOR'S BEHALF, THE ETHICAL COMMITTEE AND THE REGULATORY AUTHORITIES WILL NOT NEED MY PERMISSION TO LOOK AT MY HEALTH RECORDS, BOTH IN RESPECT OF CURRENT STUDY AND ANY FURTHER RESEARCH THAT MAY BE CONDUCTED IN RELATION TO IT, EVEN IF I WITHDRAW FROM THE STUDY I AGREE TO THIS ACCESS. HOWEVER, I UNDERSTAND THAT MY IDENTITY WILL NOT BE REVEALED IN ANY INFORMATION RELEASED TO THIRD PARTIES OR PUBLISHED, UNLESS AS REQUIRED UNDER THE LAW. I AGREE NOT TO RESTRICT THE USE OF ANY DATA OR RESULTS THAT ARISE FROM THIS STUDY.

☐ I AGREE TO TAKE PART IN THE ABOVE STUDY AND TO COMPLY WITH THE INSTRUCTIONS GIVEN DURING THE STUDY AND FAITHFULLY COOPERATE WITH THE STUDY TEAM AND TO IMMEDIATELY INFORM THE STUDY STAFF IF I SUFFER FROM ANY DETERIORATION IN MY HEALTH OR WELL-BEING OR ANY UNEXPECTED OR UNUSUAL SYMPTOMS.

☐ I HEREBY CONSENT TO PARTICIPATE IN THIS STUDY.

☐ I HEREBY GIVE PERMISSION TO UNDERGO COMPLETE CLINICAL EXAMINATION AND DIAGNOSTIC TESTS INCLUDING HEMATOLOGICAL, BIOCHEMICAL, RADIOLOGICAL TESTS.

SIGNATURE/THUMB IMPRESSION:

PATIENTS NAME AND ADDRESS: PLACE DATE

SIGNATURE OF INVESTIGATOR:

STUDY INVESTIGATOR'S NAME: PLACEDATE

MASTER CHART

1	sex	BMI	WC	WHR	SMOKING	SBP	DBP	FBS	PPBS	FASTING I	T.CHOL	TGL	HDL	LDL	HOMA IR	TYG	INSULIN R	METABOLI	CAROTID I	USG
2	M	28.34	101	1.01	+	130	90	119	210	15.81	221	168	16	138	4.6	9.21	+	+		
3	M	29.12	105	1.08	+	120	76	118	167	13.69	246	143	26	140	4.2	9.04	+	-	1MM	
4	F	31.66	108	0.91	+	132	82	122	144	16	201	180	20	152	4.8	9.3	+	-	-	
5	M	21.08	91	0.8	-	140	86	90	98	6.36	136	100	34	99	1.4	8.41	-	-		
6	M	27.44	103	1.1	+	120	82	90	106	8.18	165	98	40	92	1.8	8.39	-	-		
7	F	27.8	103	1.1		130	88	167	248	12.49	231	213	22	161	5.1	9.79	+	+	1MM	
8	F	30.02	105	1.06	_	140	90	136	223	17.44	228	266	21	158	5.8	9.8	+	+		fatty liver
9	F	28.73	104	1.07		130	82	155	179	16.09	223	188	26	138	6.1	9.59	+	+	2MM	
10	M	22.07	96	0.87	+	126	82	78	90	11.07	152	102	28	100	2.1	8.29	-	-		
11	M	30.06	106	1.07	+	128	84	206	338	10.31	241	231	28	141	5.2	10.12	+	-	2MM	
12	M	28	101	1.06	-	122	82	155	189	12.09	210	198	18	151	4.7	9.7	+	-		
13	M	24.16	95	0.81	+	120	80	78	104	9.96	146	96	30	102	1.9	8.65	-	-		
14	F	27.33	107	1.02	-	130	86	240	280	8.69	208	303	24	162	5.1	10.13	+	-	3MM	fatty liver
15	M	29.09	105	1.01	+	132	84	189	214	10.31	206	214	25	147	4.8	9.88	+	-	1MM	
16	F	23.18	94	0.7	-	110	70	108	166	7.9	158	106	32	96	2.1	9.05	-	-		
17	M	30.48	102	1.06	+	130	76	138	168	12.74	227	155	27	145	4.3	9.66	+	-		
18	F	22.19	98	0.72	-	120	82	92	98	8.89	152	88	40	95	2	8.85	-	-		
19	F	31.43	101	0.98	-	110	76	178	189	11.03	231	240	19	138	4.8	9.93	+	-		fatty liver
20	M	20.06	99	0.86	-	120	82	100	104	11.22	142	98	38	91	1.4	8.87	-	-	1MM	
21	M	21.44	98	1.02	+	126	78	108	110	10.6	160	162	48	102	2.8	9.08	+	-	1MM	
22	F	28.6	101	1.008	-	130	80	107	139	14.5	215	199	16	134	3.8	9.35	+	-		
23	F	31.3	108	1.04	-	132	84	133	167	12.9	222	88	22	167	4.2	9.6	+	-		
24	M	20.1	91	0.78	-	140	90	89	80	6.5	136	67	30	159	1.4	8.71	-	+		
25	M	28	106	1.02	+	126	84	234	267	10.1	232	98	18	199	5.8	10.21	+	-	3MM	fatty liver
26	M	24.9	100	0.8	-	116	80	56	97	11.68	141	77	31	103	1.6	8.28	-	-		
27	M	21.8	93	0.9	-	122	78	108	118	7.95	152	177	38	100	2.1	9.01	-	-		
28	M	30.2	107	1.08	+	130	80	167	159	11.76	236	412	27	139	4.8	9.89	+	-		
29	F	31.1	104	1.12	-	120	76	218	233	8.6	241	233	29	142	4.6	10.18	+	-	25% BLOCK	
30	M	22.6	92	0.92	-	118	80	79	106	9.41	163	125	32	98	1.8	8.77	-	-		

31	M	29.4	105	1.08	+	124	84	134	168	12.21	238	178	18	158	4	9.39	+	-			
32	F	30.1	100	0.91		130	86	155	189	10.8	233	298	20	149	4.1	10.05	+	-	1MM	fatty liver	
33	M	24.8	96	0.94	-	150	96	170	190	4.81	154	266	46	106	2	10.03	-	+			
34	F	23.2	99	1.03	-	148	98	90	98	8.63	148	94	53	97	1.9	8.35	-	+			
35	M	31	101	1.09	-	130	84	180	168	10.68	237	264	19	138	4.7	9.97	+	-	1MM		
36	M	30.1	103	1.08	+	122	82	130	158	14.47	153	138	23	143	4.6	9.1	+	-			
37	M	22.2	90	1.004	-	124	88	90	108	7.7	148	86	28	165	1.7	8.26	-	-			
38	M	28.4	102	1.06	+	160	100	168	176	9.98	242	246	26	151	4.1	9.94	+	+	3MM		
39	M	28.5	106	1.07	-	140	88	98	108	7.51	214	99	23	142	1.8	8.49	+	+			
40	M	25.4	92	1.03	-	150	90	112	132	7.67	152	184	44	92	2.1	9.24	-	+			
41	M	26.6	90	0.88	-	130	86	126	148	12.66	134	256	25	101	3.9	9.69	+	-			
42	M	21.5	92	0.91	+	1132	82	88	98	8.8	141	64	54	101	1.9	7.94	-	-			
43	F	22.6	88	0.88	-	130	84	70	100	9.3	151	64	29	95	1.6	7.71	-	-			
44	F	28.4	101	0.96	-	120	82	199	218	12.5	224	312	24	151	6.1	10.34	+	-	3MM		
45	F	30.1	106	1	-	114	76	134	150	13.7	231	168	22	161	4.5	9.33	+	-			
46	F	31.2	103	0.99	-	126	84	108	110	14.77	239	104	20	148	3.9	8.63	+	-	2MM		
47	F	32	105	0.97	-	118	80	133	145	11.38	217	238	18	139	3.7	9.67	+	-			
48	F	22.8	94	1.08	-	136	88	86	98	7.13	132	92	32	100	1.5	8.28	-	-			
49	M	28	101	1.03	+	120	80	198	233	10.95	228	244	17	145	5.3	10.09	+	-	2MM		
50	M	21.8	95	1.11	+	130	86	100	105	6.95	134	118	32	98	1.7	8.68	-	-			
51	M	29.6	100	1.99	+	140	84	187	159	12.68	252	288	21	168	5.8	10.2	+	-	2MM	fatty liver	
52	M	22.8	96	1.11	+	150	90	100	106	6.5	147	94	35	101	1.6	8.46	-	+			
53	M	23.4	95	0.95	-	124	78	60	108	12.27	151	88	39	101	1.8	7.88	-	-			
54	F	30	107	1.02	-	130	96	168	198	11.44	241	175	23	143	4.7	9.6	+	-	2MM		
55	M	30.6	106	1.09	+	140	86	177	149	9.97	218	94	22	152	4.3	9.03	+	+			
56	F	22.1	99	0.96	-	136	88	103	122	7.55	154	156	38	99	1.9	8.99	-	-			
57	F	29.1	103	0.94	-	120	78	109	188	15.4	225	264	21	141	4.1	8.99	+	-	1MM		
58	F	20.8	92	0.99	-	130	82	104	110	8.26	156	90	36	102	2.1	8.45	-	-			
59	F	28.6	104	0.97	-	140	90	239	277	8.73	231	148	19	147	5.1	9.78	+	+	1MM		
60	M	21.2	93	0.94	+	130	86	106	119	6.5	158	68	37	104	1.7	8.19	-	-			

61	M	28.1	105	1.2	+	132	88	166	196	12.81	239	247	18	159	5.2	9.93	+	-		
62	M	28.2	99	1.02	+	124	80	109	137	13.51	200	280	15	138	3.6	9.63	+	-		
63	F	32.1	0.1	0.98	-	122	82	279	345	8.944	248	138	27	142	6.1	9.87	+	-	2MM	fatty liver
64	F	21.1	91.2	0.72	-	118	76	80	98	7.15	135	56	28	98	1.4	7.71	-	-		
65	M	23.9	99	0.88	-	136	94	109	133	8.25	155	78	55	100	2.2	8.35	-	-		
66	F	27.3	99.6	1.01	+	120	80	213	222	8.06	202	186	22	149	4.2	9.89	+	-		
67	M	32	101.3	0.99	-	166	102	209	312	9.003	245	212	21	134	4.6	10.01	+	+	2MM	
68	F	22.1	99	0.76	-	130	80	92	114	7.114	137	88	29	88	1.6	8.31	-	-		
69	M	22.4	95.6	0.89	-	132	86	94	112	9.139	152	104	53	101	2.1	8.49	+	-		
70	M	27.5	100.1	1.06	+	130	88	123	134	12.971	204	156	16	150	3.9	9.17	+	-	1MM	
71	M	31.8	94.8	0.9	-	140	86	136	149	5.113	139	138	31	98	1.7	9.15	_	+		
72	M	31.8	102	1.08	+	120	76	99	106	21.489	243	78	26	139	5.2	8.26	+	-		
73	F	23.2	96.2	0.8	-	118	82	109	112	7.506	155	108	51	102	2	8.68	-	-		
74	F	28.6	101	1.01	-	124	80	167	189	12.215	206	243	17	148	5.1	9.92	+	-	3MM	
75	F	21.87	98.2	0.78	-	128	82	98	98	7.51	141	85	33	104	1.8	8.33	+	-		
76	M	30.6	99	1.02	+	132	80	148	198	13.26	240	138	25	158	4.8	9.23	+	-		fatty liver
77	F	22.8	97.3	0.72	-	140	88	104	124	7.47	149	154	49	101	1.9	8.99	-	+		
78	F	29.7	98	0.93	-	140	86	233	245	7.72	208	276	18	159	4.4	10.38	+	+	3MM	
79	F	23.6	94	0.88	-	150	96	88	102	7.9	140	94	35	100	1.7	8.33	-	+		
80	M	22.8	99.6	0.89	+	140	90	57	90	10.04	150	84	47	99	1.4	7.78	-	+		
81	F	23.8	99.4	0.78	-	120	72	89	80	7.35	151	48	32	98	1.6	7.67	+	-		
82	F	29.6	99.6	0.98	-	130	82	132	145	14.566	238	186	16	160	4.7	9.42	+	-	1MM	
83	M	31.5	105.8	1.09	+	126	80	167	189	10.533	209	174	26	152	4.3	9.58	+	-		
84	M	23.4	99.1	0.96	+	128	80	85	100	8.663	148	188	36	101	1.8	8.99	-	-		
85	M	29.8	104.6	1.06	-	130	90	266	289	8.766	211	217	17	148	5.7	10.27	+	-	3MM	
86	F	30.2	103.4	0.92	-	130	92	380	416	6.45	237	404	25	149	6	11.25	+	-		
87	F	23.2	94.8	0.72	-	120	82	106	110	6.174	147	104	48	103	1.6	8.61	-	-		
88	F	29.5	103.2	0.91	-	132	84	231	277	9.2	213	188	18	152	5.2	9.99	+	-	2MM	
89	F	30.1	102.1	0.94	-	128	82	210	230	9.35	235	74	24	157	4.8	8.96	+	-		
90	M	22.4	93.9	0.94	-	134	86	106	110	6.56	149	168	36	98	1.7	9.09	-	-		

91	M	29.4	101.8	1.01	-	140	98	166	189	11.58	215	105	19	143	4.7	9.07	+	+			
92	M	29.3	102.6	1.01	+	142	82	190	245	11.19	233	184	23	166	5.2	9.77	+	+	2MM		
93	M	29	103.8	1.06	-	136	90	185	214	10.17	216	266	22	150	4.6	10.11	+	-	3MM		
94	F	23.3	94.4	0.7	-	130	80	105	118	7.01	154	104	47	99	1.8	8.61	-	-			
95	M	30.2	106.3	1.1	-	142	80	245	267	8.84	236	206	21	148	5.3	10.14	+	-	2MM		
96	M	29.7	107.1	1.08	+	146	90	230	268	9.78	238	218	20	152	5.5	10.22	+	+	2MM	fatty liver	
97	M	23.1	94.4	0.8	-	130	80	104	116	7.3	154	108	38	100	1.9	8.63	-	-			
98	M	28.6	106.1	1.06	+	126	82	214	226	9.36	239	278	21	154	4.9	10.3	+	-	3MM		
99	M	29.7	103.9	1.01	+	130	80	178	218	10.8	234	204	22	149	4.7	9.81	+	-			
100	M	24	94.5	0.9	-	120	82	190	189	4.73	152	142	46	101	2.2	9.51	-	-	2MM		
101	M	28.4	103.4	0.8	+	124	84	234	245	9.09	233	268	21	152	5.2	10.35	+	-		fatty liver	
102	M	27.8	100.6	1.06	+	140	86	165	187	8.667	210	182	16	168	3.5	9.62	+	+			
103	M	31.8	107.8	1.08	-	166	96	314	389	8.4	246	138	28	160	6.6	9.98	+	-	1MM		
104	M	30.5	106.9	1.1	-	130	82	187	190	8.09	236	312	18	152	3.6	10.28	+	-		fatty liver	
105	M	20.6	90.6	0.86	-	126	80	215	237	2.66	151	206	32	99	1.4	10.01	-	-	1MM		
106	F	28.8	106.5	0.98	-	130	78	205	207	11.37	224	188	19	156	5.8	9.87	+	-			
107	F	28.9	105.4	0.93	-	126	84	174	188	11.64	238	129	26	152	4.1	9.33	+	-			
108	F	30.1	101.8	0.92	-	128	82	182	216	9.44	232	158	24	149	4.2	9.57	-	-			
109	F	23.1	92.8	0.72	-	130	90	160	178	4.5	161	163	34	101	1.8	9.48	-	-	1MM		
110	M	21.2	93.6	0.81	-	128	80	103	110	7.94	156	104	40	98	2	8.59	-	-			
111	M	22.3	96.6	1.83	+	126	81	92	97	7.11	158	66	42	99	1.6	8.02	-	-			
112	M	30.2	106	1.12	+	128	80	128	146	12.7	240	108	22	162	4	8.84	+	-			
113	F	29.7	94.6	0.76	-	126	80	123	138	4.99	148	64	36	100	1.5	8.28	-	-			
114	F	22.2	98.1	0.68	-	120	80	106	112	6.77	152	68	46	103	1.6	8.19	+	-			
115	M	23	97.3	0.71	+	140	88	98	106	7.59	142	88	37	101	1.8	8.37	-	+			
116	M	28.7	105.9	1.06	-	170	100	165	196	12.12	242	248	21	148	4.7	9.93	+	+			
117	M	28.8	104.8	1.02	+	150	90	213	275	10.75	246	326	22	156	5.6	10.46	+	+	2MM	fatty liver	
118	F	22.4	98.2	0.79	-	124	82	112	132	6.2	141	118	37	102	1.7	8.8	-	-			
119	F	23.6	98.9	0.8	-	116	76	128	146	6.39	150	162	48	101	2	9.25	-	-	1MM		
120	F	29.2	104.9	1.09	-	130	86	238	268	8.47	232	276	20	159	5.2	10.4	+	-	2MM		